	Mol Endocrinol, 13(8):1305-	section below) dyslinidemia
	17 (1999); Filipsson, K., et al.,	endocrine disorders (as
	Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
	(1998); Olson, L.K., et al., J	Disorders" section below),
	Biol Chem, 271(28):16544-52	neuropathy, vision impairment
	(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
	Journal of Biomolecular	blindness), ulcers and impaired
	Screening, 4:193-204 (1999),	wound healing, and infection
	the contents of each of which	(e.g., infectious diseases and
	is herein incorporated by	disorders as described in the
	reference in its entirety.	"Infectious Diseases" section
	Pancreatic cells that may be	below, especially of the
	used according to these assays	urinary tract and skin), carpal
	are publicly available (e.g.,	tunnel syndrome and
	through the ATCC) and/or	Dupuytren's contracture).
•	may be routinely generated.	An additional highly preferred
	Exemplary pancreatic cells that	indication is obesity and/or
	may be used according to these	complications associated with
	assays include HITT15 Cells.	obesity. Additional highly
	HITT15 are an adherent	preferred indications include
-	epithelial cell line established	weight loss or alternatively,
	from Syrian hamster islet cells	weight gain. Additional highly
	transformed with SV40. These	preferred indications are
	cells express glucagon,	complications associated with
	somatostatin, and	insulin resistance.
	glucocorticoid receptors. The	
	cells secrete insulin, which is	
	stimulated by glucose and	
	glucagon and suppressed by	
	somatostatin or	
	glucocorticoids. ATTC# CRL-	

			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
			4339-4343, 1981.	
HNFJF07	731	Regulation of	Assays for the regulation of	A highly preferred indication
		transcription via	transcription through the	is diabetes mellitus.
		DMEF1 response	DMEF1 response element are	Additional highly preferred
		element in	well-known in the art and may	indications include
		adipocytes and pre-	be used or routinely modified	complications associated with
		adipocytes	to assess the ability of	diabetes (e.g., diabetic
			polypeptides of the invention	retinopathy, diabetic
			(including antibodies and	nephropathy, kidney disease
			agonists or antagonists of the	(e.g., renal failure,
			invention) to activate the	nephropathy and/or other
			DMEF1 response element in a	diseases and disorders as
			reporter construct (such as that	described in the "Renal
			containing the GLUT4	Disorders" section below),
			promoter) and to regulate	diabetic neuropathy, nerve
			insulin production. The	disease and nerve damage
			DMEF1 response element is	(e.g., due to diabetic
			present in the GLUT4	neuropathy), blood vessel
			promoter and binds to MEF2	blockage, heart disease, stroke,
			transcription factor and another	impotence (e.g., due to diabetic
			transcription factor that is	neuropathy or blood vessel
			required for insulin regulation	blockage), seizures, mental
			of Glut4 expression in skeletal	confusion, drowsiness,
			muscle. GLUT4 is the primary	nonketotic hyperglycemic-
			insulin-responsive glucose	hyperosmolar coma,
			transporter in fat and muscle	cardiovascular disease (e.g.,
			tissue. Exemplary assays that	heart disease, atherosclerosis,

may be used or routinely	microvascular disease.
modified to test for DMEF1	hypertension, stroke, and other
 response element activity (in	diseases and disorders as
 adipocytes and pre-adipocytes)	described in the
by polypeptides of the	"Cardiovascular Disorders"
invention (including antibodies	section below), dyslipidemia,
 and agonists or antagonists of	
 the invention) include assays	described in the "Endocrine
 disclosed inThai, M.V., et al., J	
 Biol Chem, 273(23):14285-92	neuropathy, vision impairment
 (1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
 Chem, 275(21):16323-8	blindness), ulcers and impaired
 (2000); Liu, M.L., et al., J Biol	
 Chem, 269(45):28514-21	
(1994); "Identification of a 30-	disorders as described in the
base pair regulatory element	"Infectious Diseases" section
and novel DNA binding	below, especially of the
protein that regulates the	urinary tract and skin). An
human GLUT4 promoter in	additional highly preferred
 transgenic mice", J Biol Chem.	
 2000 Aug 4;275(31):23666-73;	complications associated with
 Berger, et al., Gene 66:1-10	obesity. Additional highly
 (1988); and, Cullen, B., et al.,	preferred indications include
 Methods in Enzymol.	weight loss or alternatively,
 216:362–368 (1992), the	weight gain. Additional highly
 contents of each of which is	preferred indications are
herein incorporated by	complications associated with
 reference in its entirety.	insulin resistance.
 Adipocytes and pre-adipocytes	
 that may be used according to	
these assays are publicly	

			available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3	
			clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	
HNFJF07	731	Regulation of viability and proliferation of	Assays for the regulation of viability and proliferation of cells in vitro are well-known in	A highly preferred indication is diabetes mellitus. An additional highly preferred
		pancreatic beta cells.	the art and may be used or routinely modified to assess the ability of polypeptides of	indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic
	÷		antibodies and agonists or antagonists of the invention) to regulate viability and	nephropauny, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as
			proliferation of pancreatic beta cells. For example, the Cell	described in the "Renal Disorders" section below), diabetic neuronathy nerve
			viability assay measures the number of viable cells in	disease and nerve damage (e.g., due to diabetic

		culture based on quantitation	neuropathy), blood vessel
		of the ATP present which	blockage, heart disease, stroke,
<u> </u>		signals the presence of	impotence (e.g., due to diabetic
		metabolically active cells.	neuropathy or blood vessel
		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
		test regulation of viability and	nonketotic hyperglycemic-
		proliferation of pancreatic beta	hyperosmolar coma,
		cells by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Friedrichsen BN,	diseases and disorders as
		et al., Mol Endocrinol,	described in the
		15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
		MA, et al., Endocrinology,	section below), dyslipidemia,
		139(4):1494-9 (1998); Hugl	endocrine disorders (as
	_	SR, et al., J Biol Chem 1998	described in the "Endocrine
		Jul 10;273(28):17771-9	Disorders" section below),
		(1998), the contents of each of	neuropathy, vision impairment
		which is herein incorporated	(e.g., diabetic retinopathy and
		by reference in its entirety.	blindness), ulcers and impaired
		Pancreatic cells that may be	wound healing, and infection
		used according to these assays	(e.g., infectious diseases and
		are publicly available (e.g.,	disorders as described in the
		through the ATCC) and/or	"Infectious Diseases" section
		may be routinely generated.	below, especially of the
		Exemplary pancreatic cells that	urinary tract and skin), carpal
		may be used according to these	tunnel syndrome and
		assays include rat INS-1 cells.	Dupuytren's contracture). An
		INS-1 cells are a semi-	additional highly preferred

			adherent cell line established	indication is obesity and/or
			from cells isolated from an X-	complications associated with
			ray induced rat transplantable	obesity. Additional highly
			insulinoma. These cells retain	preferred indications include
			characteristics typical of native	weight loss or alternatively,
			pancreatic beta cells including	weight gain. Additional highly
 			glucose inducible insulin	preferred indications are
			secretion. References: Asfari	complications associated with
			et al. Endocrinology 1992	insulin resistance.
			130:167.	
HNFJF07	731	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate the serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth. Exemplary assays	Activity", "Blood-Related
			for transcription through the	Disorders", and/or
			SRE that may be used or	"Cardiovascular Disorders"),
			routinely modified to test SRE	Highly preferred indications
			activity of the polypeptides of	include autoimmune diseases
			the invention (including	(e.g., rheumatoid arthritis,
			antibodies and agonists or	systemic lupus erythematosis,
			antagonists of the invention)	Crohn"s disease, multiple

sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional	highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases	(e.g., teukemia, 1ymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include
include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362- 368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and	Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary mouse 1 cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.

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_				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
	-			plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
	-			arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
			-	cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HNFJF07	731	Stimulation of	Assays for measuring secretion	A highly preferred
		insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
		from pancreatic	the art and may be used or	An additional highly preferred

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nplicatio	abetes (e	ıy, diabe	ey disea		or other	ders as	Renal	(wolad	iy, nerve	damage	tic	d vessel	sease, sti	ue to dia	od vesse	s, menta	ness,	lycemic	la,	ease (e.g	rosclero	ease,	ke, and o	ders as		isorders	rslipiden	rs (as	Endocrir	below)
is a con	with di	tinopath	hy, kidn	l failure	hy and/c	nd disor	in the "I	' section	europath	d nerve	to diabe	y), bloo	heart di	e.g., d	y or bloo	, seizure	, drowsi	hyperg	olar con	cular dis	ase, athe	ular dise	ion, stro	nd disor	in the	scular D	low), dy	disorde	in the "I	'section
indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),
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d to asse	peptides	luding	onists or	inventic	secretion	ılin secre	MAT usi	tibodies.	from	lls is	ucose an		and	key	betes.	that ma	modifie	n of insu	ancreatic	ides of t	ng antib	itagonist	lude ass	en, B., et	7(4 Pt); Li, M	γ,	1997); K	S. Lett,	95); and,
modifie	y of poly	tion (inc	s and ag	ts of the	insulin s	ple, insu	ed by Fl	isulin an	cretion 1	c beta ce	ed by gl	ertain	eptides,	tion is a	nt in dial	y assays	outinely	imulatio	(from pa	polypept	(includi	ists or ar	tion) inc	in: Ahre	/siol, 27	96 (1996	crinolog	735-40 (II, FEBS	32-9 (199
routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	stimulate insulin secretion.	For example, insulin secretion	is measured by FMAT using	anti-rat insulin antibodies.	Insulin secretion from	pancreatic beta cells is	upregulated by glucose and	also by certain	proteins/peptides, and	disregulation is a key	component in diabetes.	Exemplary assays that may be	used or routinely modified to	test for stimulation of insulin	secretion (from pancreatic	cells) by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Ahren, B., et al.,	Am J Physiol, 277(4 Pt	2):R959-66 (1999); Li, M., et	al., Endocrinology,	138(9):3735-40 (1997); Kim,	K.H., et al., FEBS Lett,	377(2):237-9 (1995); and,
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ells.																														
beta cells.																														
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				Miraelia S et. al Journal of	neuropathy, vision impairment
				Biomolecular Screening,	(e.g., diabetic retinopathy and
				4:193-204 (1999), the contents	blindness), ulcers and impaired
				of each of which is herein	wound healing, and infection
				incorporated by reference in its	(e.g., infectious diseases and
				entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
				assays are publicly available	below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
				pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
_				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
_				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HNGAK47	732	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
			Apoptosis	caspase apoptosis are well	embodiment of the invention
				known in the art and may be	includes a method for
				used or routinely modified to	stimulating endothelial cell
				assess the ability of	growth. An alternative highly
				polypeptides of the invention	preferred embodiment of the

 (including antibodies and	invention includes a method
agonists or antagonists of the	for inhibiting endothelial cell
invention) to promote caspase	growth. A highly preferred
 protease-mediated apoptosis.	embodiment of the invention
Induction of apoptosis in	includes a method for
endothelial cells supporting the	stimulating endothelial cell
vasculature of tumors is	proliferation. An alternative
associated with tumor	highly preferred embodiment
regression due to loss of tumor	of the invention includes a
blood supply. Exemplary	method for inhibiting
 assays for caspase apoptosis	endothelial cell proliferation.
that may be used or routinely	A highly preferred
modified to test capase	embodiment of the invention
apoptosis activity of	includes a method for
 polypeptides of the invention	stimulating apoptosis of
 (including antibodies and	endothelial cells. An
agonists or antagonists of the	alternative highly preferred
invention) include the assays	embodiment of the invention
disclosed in Lee et al., FEBS	includes a method for
Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
 209-218 (2000); and Karsan	A highly preferred
and Harlan, J Atheroscler	embodiment of the invention
Thromb 3(2): 75-80 (1996);	includes a method for
the contents of each of which	stimulating angiogenisis. An
are herein incorporated by	alternative highly preferred
 reference in its entirety.	embodiment of the invention
Endothelial cells that may be	includes a method for
 used according to these assays	inhibiting angiogenesis. A
 are publicly available (e.g.,	highly preferred embodiment
through commercial sources).	of the invention includes a

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method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels
Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																			
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such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,
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pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Highly preferred indications also include arterial disease,	such as, atherosclerosis, hypertension, coronary artery	disease, inflammatory vasculitides, Reynaud"s	disease and Reynaud"s phenomenom, aneurysms.	restenosis; venous and	lymphatic disorders such as thrombophlebitis,	lymphangitis, and	lymphedema; and other	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and
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lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of
	Activation of transcription through serum response element in immune cells (such as T-cells).
	732
	HNGAK47

the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	the the second s
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esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma. Burkitt's lymphoma.	arthritis, AIDS, granulomatous disease, inflammatory bowel	disease, neutropenia, neutrophilia, psoriasis, suppression of immune	reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,	meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An	additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
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	HNGBC07	733	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
		_		the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
		-		expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
_		-		transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
			-	disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and
				Malm, Methods in Enzymol	suppressing a T cell-mediated
		-		216:362-368 (1992); Henthorn	immune response. Additional
		354		et al., Proc Natl Acad Sci USA	highly preferred indications
				85:6342-6346 (1988); Benson	include inflammation and
				et al., J Immunol 153(9):3862-	inflammatory disorders, and

3873 (1994	II.,	treating joint damage in
Virus Gen		patients with rheumatoid
(1997), the		arthritis. An additional highly
which are		preferred indication is sepsis.
by reference	by reference in its entirety. T	Highly preferred indications
cells that n	cells that may be used	include neoplastic diseases
according	s are	(e.g., leukemia, lymphoma,
publicly av		and/or as described below
through the ATCC)		under "Hyperproliferative
Exemplary	Exemplary T cells that may be	Disorders"). Additionally,
used accor		highly preferred indications
include the		include neoplasms and
which is a	which is a human natural killer	cancers, such as, for example,
cell line w	cell line with cytolytic and	leukemia, lymphoma,
cytotoxic activity.		melanoma, glioma (e.g.,
		malignant glioma), solid
	-	tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),

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plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
plasmacytomas, multiple myeloma, Burkitt's lympho arthritis, AIDS, granulomat disease, inflammatory bow disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemoph hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, asthma and allergy. An additional preferred indicat is infection (e.g., an infectiudisease as described below under "Infectious Disease".	
plasmacytomas, mul myeloma, Burkitt's arthritis, AIDS, grar disease, inflammato disease, inflammato disease, neutropenia neutrophilia, psorias suppression of imm reactions to transpla organs and tissues, I hypercoagulation, d mellitus, endocardit meningitis, Lyme D cardiac reperfusion asthma and allergy. additional preferred is infection (e.g., an disease as described under "Infectious D	
plasme myelor arthriti disease disease neutro suppre reactic organs hyperc menin menin cardia asthma additic is infe disease under	
	of of wn in r ss sof on) to
	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For
	Assays for the regulation increases or decreases) or viability and proliferation cells in vitro are well-kn the art and may be used routinely modified to assthe ability of polypeptid the invention (including antibodies and agonists of antagonists of the inventregulate viability and proliferation of pre-adipocells and cell lines. For
	ys for tasses or asses or llity and in vitra and in nely moly molity of nitro ordies a gonists genists and ce and ce and ce and ce and ce
	Assa incre viabi cells the a routi the a the in antib antage regul prolit cells
	of pre- (such lls)
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	Prolife adipos as 3T3
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	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention
example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127- 133 (1974), which is herein incorporated by reference in its	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or
	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	734
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			antagonists of the invention) to includes a method for	includes a method for
-			promote or inhibit cell	stimulating endothelial cell
			proliferation, activation, and	proliferation. An alternative
			apoptosis. Exemplary assays	highly preferred embodiment
			for JNK and p38 kinase	of the invention includes a
			activity that may be used or	method for inhibiting
			routinely modified to test JNK	endothelial cell proliferation.
			and p38 kinase-induced	A highly preferred
			activity of polypeptides of the	embodiment of the invention
			invention (including antibodies	includes a method for
			and agonists or antagonists of	stimulating apoptosis of
			the invention) include the	endothelial cells. An
			assays disclosed in Forrer et	alternative highly preferred
			al., Biol Chem 379(8-9):1101-	embodiment of the invention
			1110 (1998); Gupta et al., Exp	includes a method for
			Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
		•	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
			Soc Symp 64:29-48 (1999);	A highly preferred
			Chang and Karin, Nature	embodiment of the invention
			410(6824):37-40 (2001); and	includes a method for
_			Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
			Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
			the contents of each of which	alternative highly preferred
			are herein incorporated by	embodiment of the invention
			reference in its entirety.	includes a method for
-			Endothelial cells that may be	inhibiting (e.g., decreasing) the
			used according to these assays	activation of and/or
			are publicly available (e.g.,	inactivating endothelial cells.
			through the ATCC).	A highly preferred
			Exemplary endothelial cells	embodiment of the invention
			that may be used according to	includes a method for

	 these assays include human	stimulating angiogenisis. An
	umbilical vein endothelial cells	alternative highly preferred
	(HUVEC), which are	embodiment of the invention
	endothelial cells which line	includes a method for
	venous blood vessels, and are	inhibiting angiogenesis. A
	involved in functions that	highly preferred embodiment
_	include, but are not limited to,	of the invention includes a
	angiogenesis, vascular	method for reducing cardiac
	permeability, vascular tone,	hypertrophy. An alternative
	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as
		described below under
		"Hyperproliferative
		Disorders"), and disorders of
		the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
		aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
		and atherosclerotic vascular
		disease, diabetic nephropathy,
		intracardiac shunt, cardiac
		hypertrophy, myocardial
	-	infarction, chronic
		hemodynamic overload, and/or

as described below under "Cardiovascular Disorders").	Highly preferred indications	include cardiovascular, endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,
							-		-																-	. ,	

angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign	dysproliterative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery	disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer.

			preferred indications also
			include trauma such as
-			wounds, burns, and injured
			tissue (e.g., vascular injury
			such as, injury resulting from
			balloon angioplasty, and
			atheroschlerotic lesions),
			implant fixation, scarring,
			ischemia reperfusion injury,
	•		rheumatoid arthritis,
			cerebrovascular disease, renal
			diseases such as acute renal
			failure, and osteoporosis.
			Additional highly preferred
			indications include stroke,
			graft rejection, diabetic or
			other retinopathies, thrombotic
			and coagulative disorders,
			vascularitis, lymph
		-	angiogenesis, sexual disorders,
	•		age-related macular
-			degeneration, and treatment
			/prevention of endometriosis
		****	and related conditions.
		•	Additional highly preferred
			indications include fibromas,
			heart disease, cardiac arrest,
			heart valve disease, and
			vascular disease.
			Preferred indications include
			blood disorders (e.g., as

		3	factors and modulate the	disorders (e.g., as described
		i (1)	expression of genes involved	below under "Immune
		<u> </u>	in growth. Exemplary assays	Activity", "Blood-Related
		¥	for transcription through the	Disorders", and/or
 		S	SRE that may be used or	"Cardiovascular Disorders"),
		<u> </u>	routinely modified to test SRE	Highly preferred indications
 	-	<u> </u>	activity of the polypeptides of	include autoimmune diseases
			the invention (including	(e.g., rheumatoid arthritis,
			antibodies and agonists or	systemic lupus erythematosis,
 			antagonists of the invention)	Crohn"s disease, multiple
		<u>.:</u>	include assays disclosed in	sclerosis and/or as described
		<u> </u>	Berger et al., Gene 66:1-10	below), immunodeficiencies
			(1998); Cullen and Malm,	(e.g., as described below),
			Methods in Enzymol 216:362-	boosting a T cell-mediated
		3	368 (1992); Henthorn et al.,	immune response, and
		1	Proc Natl Acad Sci USA	suppressing a T cell-mediated
			85:6342-6346 (1988); and	immune response. Additional
		I	Black et al., Virus Genes	highly preferred indications
			12(2):105-117 (1997), the	include inflammation and
 _		3	content of each of which are	inflammatory disorders, and
•			herein incorporated by	treating joint damage in
		+	reference in its entirety. T	patients with rheumatoid
		<u> </u>	cells that may be used	arthritis. An additional highly
		,	according to these assays are	preferred indication is sepsis.
			publicly available (e.g.,	Highly preferred indications
_		1	through the ATCC).	include neoplastic diseases
		<u> </u>	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
		<u> </u>	may be used according to these	and/or as described below
			assays include the CTLL cell	under "Hyperproliferative
	-		line, which is an IL-2	Disorders"). Additionally,
)	dependent suspension culture	highly preferred indications

of T cells with cytotoxic	include neoplasms and
activity.	cancers, such as, for example,
	leukemia, lymphoma,
	melanoma, glioma (e.g.,
	malignant glioma), solid
	tumors, and prostate, breast,
	lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver and urinary cancer. Other
 	preferred indications include
	benign dysproliferative
	disorders and pre-neoplastic
	conditions, such as, for
	example, hyperplasia,
	metaplasia, and/or dysplasia.
	Preferred indications include
	anemia, pancytopenia,
	leukopenia, thrombocytopenia,
	Hodgkin's disease, acute
	lymphocytic anemia (ALL),
	plasmacytomas, multiple
	myeloma, Burkitt's lymphoma,
	arthritis, AIDS, granulomatous
	disease, inflammatory bowel
	disease, neutropenia,
	neutrophilia, psoriasis,
	suppression of immune
	reactions to transplanted
	organs and tissues,
	hemophilia, hypercoagulation,
	diabetes mellitus, endocarditis,

				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HNGFR31	736	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
			of insulin are well-known in	is diabetes mellitus. An
			the art and may be used or	additional highly preferred
			routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease
			antagonists of the invention) to	(e.g., renal failure,
			stimulate insulin secretion.	nephropathy and/or other
			For example, insulin secretion	diseases and disorders as
			is measured by FMAT using	described in the "Renal
			anti-rat insulin antibodies.	Disorders" section below),
			Insulin secretion from	diabetic neuropathy, nerve
			pancreatic beta cells is	disease and nerve damage
			upregulated by glucose and	(e.g., due to diabetic
			also by certain	neuropathy), blood vessel
			proteins/peptides, and	blockage, heart disease, stroke,
			disregulation is a key	impotence (e.g., due to diabetic
			component in diabetes.	neuropathy or blood vessel
			Exemplary assays that may be	blockage), seizures, mental
			used or routinely modified to	confusion, drowsiness,
			test for stimulation of insulin	nonketotic hyperglycemic-
			secretion (from pancreatic	hyperosmolar coma,
			cells) by polypeptides of the	cardiovascular disease (e.g.,

			invention (including antibodies	heart disease, atherosclerosis,
			and agonists or antagonists of	microvascular disease,
			the invention) include assays	hypertension, stroke, and other
		,,	disclosed in: Shimizu, H., et	diseases and disorders as
			al., Endocr J, 47(3):261-9	described in the
			(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
			Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
			17 (1999); Filipsson, K., et al.,	endocrine disorders (as
			Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
			(1998); Olson, L.K., et al., J	Disorders" section below),
			Biol Chem, 271(28):16544-52	neuropathy, vision impairment
-			(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
			Journal of Biomolecular	blindness), ulcers and impaired
		-	Screening, 4:193-204 (1999),	wound healing, and infection
			the contents of each of which	(e.g., infectious diseases and
			is herein incorporated by	disorders as described in the
			reference in its entirety.	"Infectious Diseases" section
			Pancreatic cells that may be	below, especially of the
			used according to these assays	urinary tract and skin), carpal
			are publicly available (e.g.,	tunnel syndrome and
			through the ATCC) and/or	Dupuytren's contracture).
			may be routinely generated.	An additional highly preferred
	_		Exemplary pancreatic cells that	indication is obesity and/or
			may be used according to these	complications associated with
			assays include HITT15 Cells.	obesity. Additional highly
			HITT15 are an adherent	preferred indications include
			epithelial cell line established	weight loss or alternatively,
-			from Syrian hamster islet cells	weight gain. Additional highly
			transformed with SV40. These	preferred indications are
-			cells express glucagon,	complications associated with
			somatostatin, and	insulin resistance.

			glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	
HNGIJ31	737	Activation of transcription through cAMP response element in immune cells (such as T-cells).	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription texponse	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infectious disease as described below under "Infectious Disease"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below),
			element that may be used or routinely modified to test cAMP-response element	boosting a T cell-mediated immune response, and suppressing a T cell-mediated

activity of polynentides of the	immune response. Additional
invention (including antibodies	preferred indications include
and agonists or antagonists of	inflammation and
the invention) include assays	inflammatory disorders.
disclosed in Berger et al., Gene	Highly preferred indications
66:1-10 (1998); Cullen and	
Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
216:362-368 (1992); Henthorn	and/or as described below
et al., Proc Natl Acad Sci USA	under "Hyperproliferative
85:6342-6346 (1988); Black et	Disorders"). Highly preferred
al., Virus Genes 15(2):105-117	indications include neoplasms
(1997); and Belkowski et al., J	and cancers, such as, for
Immunol 161(2):659-665	example, leukemia, lymphoma
(1998), the contents of each of	(e.g., T cell lymphoma,
which are herein incorporated	Burkitt's lymphoma, non-
by reference in its entirety. T	Hodgkins lymphoma,
cells that may be used	Hodgkin"s disease),
according to these assays are	melanoma, and prostate,
publicly available (e.g.,	breast, lung, colon, pancreatic,
through the ATCC).	esophageal, stomach, brain,
Exemplary mouse T cells that	liver and urinary cancer. Other
may be used according to these	preferred indications include
assays include the CTLL cell	benign dysproliferative
line, which is a suspension	disorders and pre-neoplastic
culture of IL-2 dependent	conditions, such as, for
cytotoxic T cells.	example, hyperplasia,
	metaplasia, and/or dysplasia.
	Preferred indications include
	anemia, pancytopenia,
	leukopenia, thrombocytopenia,
	acute lymphocytic anemia

	evaluate the production of cell	Preferred indications include
-		Line of discondens (or or or
	surface markers, such as	6100d disorders (e.g., as
	monocyte chemoattractant	described below under
	protein (MCP), and the	"Immune Activity", "Blood-
	activation of monocytes and T	Related Disorders", and/or
	cells. Such assays that may be	"Cardiovascular Disorders").
	used or routinely modified to	Highly preferred indications
	test immunomodulatory and	include autoimmune diseases
	diffferentiation activity of	(e.g., rheumatoid arthritis,
	polypeptides of the invention	systemic lupus erythematosis,
	(including antibodies and	multiple sclerosis and/or as
	agonists or antagonists of the	described below) and
	invention) include assays	immunodeficiencies (e.g., as
	disclosed in Miraglia et al., J	described below). Preferred
	Biomolecular Screening 4:193-	indications also include
	204(1999); Rowland et al.,	anemia, pancytopenia,
	"Lymphocytes: a practical	leukopenia, thrombocytopenia,
	approach" Chapter 6:138-160	Hodgkin's disease, acute
	(2000); Satthaporn and	lymphocytic anemia (ALL),
	Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
	45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
	Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
	158:2919-2925 (1997), the	disease, inflammatory bowel
	contents of each of which are	disease, sepsis, neutropenia,
	herein incorporated by	neutrophilia, psoriasis,
	reference in its entirety.	suppression of immune
	Human dendritic cells that may	reactions to transplanted
	be used according to these	organs and tissues,
	assays may be isolated using	hemophilia, hypercoagulation,
	techniques disclosed herein or	diabetes mellitus, endocarditis,
	otherwise known in the art.	meningitis (bacterial and

viral), Lyme Disease, asthma, and allergy Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal
Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using
	Stimulation of insulin secretion from pancreatic beta cells.
	737
	HNGIJ31

	18	anti-rat insulin antibodies.	Disorders" section below).
		Insulin secretion from	diabetic neuropathy, nerve
			diacone medicipanty, nor ve
	<u> </u>	pancreatic beta cells is	disease and nerve damage
	in	upregulated by glucose and	(e.g., due to diabetic
	al	also by certain	neuropathy), blood vessel
	Id	proteins/peptides, and	blockage, heart disease, stroke,
	ip	disregulation is a key	impotence (e.g., due to diabetic
	33	component in diabetes.	neuropathy or blood vessel
	ш́ —	Exemplary assays that may be	blockage), seizures, mental
	in	used or routinely modified to	confusion, drowsiness,
	te	test for stimulation of insulin	nonketotic hyperglycemic-
	38	secretion (from pancreatic	hyperosmolar coma,
	3	cells) by polypeptides of the	cardiovascular disease (e.g.,
	<u> </u>	invention (including antibodies	heart disease, atherosclerosis,
	aı	and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
	ip	disclosed in: Ahren, B., et al.,	diseases and disorders as
	A	Am J Physiol, 277(4 Pt	described in the
		2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
	al	al., Endocrinology,	section below), dyslipidemia,
-		138(9):3735-40 (1997); Kim,	endocrine disorders (as
	$\overline{\lambda}$	K.H., et al., FEBS Lett,	described in the "Endocrine
	3.	377(2):237-9 (1995); and,	Disorders" section below),
-	N	Miraglia S et. al., Journal of	neuropathy, vision impairment
	B	Biomolecular Screening,	(e.g., diabetic retinopathy and
	4	4:193-204 (1999), the contents	blindness), ulcers and impaired
	TO .	of each of which is herein	wound healing, and infection
	ni	incorporated by reference in its	(e.g., infectious diseases and
	e	entirety. Pancreatic cells that	disorders as described in the
	m	may be used according to these	"Infectious Diseases" section
	as	assays are publicly available	below, especially of the

			(e.g., through the ATCC) and/or may be routinely	urinary tract and skin), carpal tunnel syndrome and
			generated. Exemplary	Dupuytren's contracture).
			pancreatic cells that may be	An additional highly preferred
		-	used according to these assays	indication is obesity and/or
			include rat INS-1 cells. INS-1	complications associated with
			cells are a semi-adherent cell	obesity. Additional highly
			line established from cells	preferred indications include
			isolated from an X-ray induced	ır alterna
			rat transplantable insulinoma.	weight gain. Aditional
			These cells retain	highly preferred indications are
			characteristics typical of native	complications associated with
			pancreatic beta cells including	insulin resistance.
			glucose inducible insulin	
			secretion. References: Asfari	
			et al. Endocrinology 1992	
			130:167.	
HNGIJ31	737	Activation of	Kinase assay. Kinase assays,	A highly preferred
		Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
		PI3 Kinase	assay, for PI3 kinase signal	includes a method for
		Signalling Pathway	transduction that regulate	increasing muscle cell survival
			glucose metabolism and cell	An alternative highly preferred
			survivial are well-known in the	embodiment of the invention
			art and may be used or	includes a method for
			routinely modified to assess	decreasing muscle cell
			the ability of polypeptides of	survival. A preferred
			the invention (including	embodiment of the invention
			antibodies and agonists or	includes a method for
			antagonists of the invention) to	stimulating muscle cell
			promote or inhibit glucose	proliferation. In a specific
			metabolism and cell survival.	embodiment, skeletal muscle

	Exemplary assays for PI3	cell proliferation is stimulated.
	kinase activity that may be	An alternative highly preferred
	 used or routinely modified to	embodiment of the invention
	test PI3 kinase-induced activity	includes a method for
	of polypeptides of the	inhibiting muscle cell
	invention (including antibodies	proliferation. In a specific
	and agonists or antagonists of	embodiment, skeletal muscle
	the invention) include assays	cell proliferation is inhibited.
	disclosed in Forrer et al., Biol	A preferred embodiment of
	Chem 379(8-9):1101-1110	the invention includes a
	(1998); Nikoulina et al.,	method for stimulating muscle
	Diabetes 49(2):263-271	cell differentiation. In a
	(2000); and Schreyer et al.,	specific embodiment, skeletal
	 Diabetes 48(8):1662-1666	muscle cell differentiation is
	(1999), the contents of each of	stimulated. An alternative
	which are herein incorporated	highly preferred embodiment
	by reference in its entirety.	of the invention includes a
	Rat myoblast cells that may be	method for inhibiting muscle
	used according to these assays	cell differentiation. In a
	are publicly available (e.g.,	specific embodiment, skeletal
	through the ATCC).	muscle cell differentiation is
	Exemplary rat myoblast cells	inhibited. Highly preferred
	that may be used according to	indications include disorders of
	these assays include L6 cells.	the musculoskeletal system.
	L6 is an adherent rat myoblast	Preferred indications include
	cell line, isolated from primary	neoplastic diseases (e.g., as
	cultures of rat thigh muscle,	described below under
	that fuses to form	"Hyperproliferative
	multinucleated myotubes and	Disorders"), endocrine
	striated fibers after culture in	disorders (e.g., as described
	differentiation media.	below under "Endocrine

Disorders"), neural disorders	(e.g., as described below under	"Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence
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(e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental	confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma, cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infections	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with
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		, ,																							

obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additonal highly preferred	indications are disorders of the	musculoskeletal system	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	failure, cachexia, myxomas,	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Highly	preferred indications include	neoplasms and cancer, such as,	rhabdomyoma,	rhabdosarcoma, stomach,	esophageal, prostate, and	urinary cancer. Preferred	indications also include breast,	lung, colon, pancreatic, brain,	and liver cancer. Other
																		***			-	_								

					preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.
14	HNGJE50	738	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is
				disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of	the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g.,
				polypeptides of the invention (including antibodies and	rheumatoid arthritis, systemic lupus erythematosis, multiple

agonists or antagonists of the sclerosis and/or as described invention) to mediate below) and	pu	ılate T	cell proliferation and function. preferred indications also	Exemplary assays that test for include boosting a B cell-	evaluate the production of and alternatively suppressing	-p	 upregulation of T cell indications include	proliferation and functional inflammation and	activities. Such assays that inflammatory	may be used or routinely disorders. Additional highly	modified to test preferred indications include	immunomodulatory and asthma and allergy. Highly	differentiation activity of preferred indications include	polypeptides of the invention neoplastic diseases (e.g.,	(including antibodies and myeloma, plasmacytoma,	the	invention) include assays melanoma, and/or as described	disclosed in Miraglia et al., J below under	<u>ئ</u> ج	204(1999); Rowland et al., Disorders"). Highly preferred	"Lymphocytes: a practical indications include neoplasms	approach" Chapter 6:138-160 and cancers, such as, myeloma,	(2000); and Verhasselt et al., J plasmacytoma, leukemia,	Immunol 158:2919-2925 lymphoma, melanoma, and	(1997), the contents of each of prostate, breast, lung, colon,	which are herein incorporated pancreatic, esophageal,
		-									-		_													

			Human dendritic cells that may be used according to these	urinary cancer. Other preferred indications include benign
			assays may be isolated using	dysproliferative disorders and
 			techniques disclosed herein or	pre-neoplastic conditions, such
 			otherwise known in the art.	as, for example, hyperplasia,
			Human dendritic cells are	metaplasia, and/or dysplasia.
			antigen presenting cells in	Preferred indications include
			suspension culture, which,	anemia, pancytopenia,
			when activated by antigen	leukopenia, thrombocytopenia,
			and/or cytokines, initiate and	Hodgkin's disease, acute
			upregulate T cell proliferation	lymphocytic anemia (ALL),
 			and functional activities.	multiple myeloma, Burkitt's
				lymphoma, arthritis, AIDS,
				granulomatous disease,
 				inflammatory bowel disease,
 				sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, and Lyme Disease.
				An additonal preferred
				indication is infection (e.g., an
 				infectious disease as described
				below under "Infectious
	!	!		Disease").
HNGJE50	738	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
			of insulin are well-known in	is diabetes mellitus. An
			the art and may be used or	additional highly preferred

да пр	routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin	indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-
	secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J	hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below),

		Biol Chem, 271(28):16544-52	neuropathy, vision impairment
		(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
		Journal of Biomolecular	blindness), ulcers and impaired
		Screening, 4:193-204 (1999),	wound healing, and infection
		the contents of each of which	(e.g., infectious diseases and
_		is herein incorporated by	disorders as described in the
		reference in its entirety.	"Infectious Diseases" section
		Pancreatic cells that may be	below, especially of the
	_	used according to these assays	urinary tract and skin), carpal
		are publicly available (e.g.,	tunnel syndrome and
		through the ATCC) and/or	Dupuytren's contracture).
		may be routinely generated.	An additional highly preferred
		Exemplary pancreatic cells that	indication is obesity and/or
		may be used according to these	complications associated with
		assays include HITT15 Cells.	obesity. Additional highly
		HITT15 are an adherent	preferred indications include
		epithelial cell line established	weight loss or alternatively,
 		from Syrian hamster islet cells	weight gain. Additional highly
		transformed with SV40. These	preferred indications are
		cells express glucagon,	complications associated with
	•	somatostatin, and	insulin resistance.
		glucocorticoid receptors. The	
		cells secrete insulin, which is	
		stimulated by glucose and	
		glucagon and suppressed by	
		somatostatin or	
		glucocorticoids. ATTC# CRL-	
 -		1777 Refs: Lord and	
•		Ashcroft. Biochem. J. 219:	
	-	547-551; Santerre et al. Proc.	
		Natl. Acad. Sci. USA 78:	

				4339-4343, 1981.	
	HNGJT54	739	Activation of	Assays for the activation of	Preferred indications include
			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described
				agonists or antagonists of the	below under "Infectious
_				invention) to increase cAMP	Disease"). Preferred
				and regulate CREB	indications include
				transcription factors, and	autoimmune diseases (e.g.,
				modulate expression of genes	rheumatoid arthritis, systemic
				involved in a wide variety of	lupus erythematosis, multiple
_			-	cell functions. Exemplary	sclerosis and/or as described
				assays for transcription	below), immunodeficiencies
			-	through the cAMP response	(e.g., as described below),
				element that may be used or	boosting a T cell-mediated
				routinely modified to test	immune response, and
				cAMP-response element	suppressing a T cell-mediated
			,	activity of polypeptides of the	immune response. Additional
				invention (including antibodies	preferred indications include
				and agonists or antagonists of	inflammation and
				the invention) include assays	inflammatory disorders.
				disclosed in Berger et al., Gene	Highly preferred indications
	-			66:1-10 (1998); Cullen and	include neoplastic diseases
				Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
				216:362-368 (1992); Henthorn	and/or as described below
				et al., Proc Natl Acad Sci USA	under "Hyperproliferative
				85:6342-6346 (1988); Black et	Disorders"). Highly preferred

				diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allerey.
HNGJT54	739	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate the serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth. Exemplary assays	Activity", "Blood-Related
			for transcription through the	Disorders", and/or
			SRE that may be used or	"Cardiovascular Disorders"),
			routinely modified to test SRE	Highly preferred indications
			activity of the polypeptides of	include autoimmune diseases
			the invention (including	(e.g., rheumatoid arthritis,
			antibodies and agonists or	systemic lupus erythematosis,
			antagonists of the invention)	Crohn"s disease, multiple
			include assays disclosed in	sclerosis and/or as described
			Berger et al., Gene 66:1-10	below), immunodeficiencies
			(1998); Cullen and Malm,	(e.g., as described below),
			Methods in Enzymol 216:362-	boosting a T cell-mediated
		-	368 (1992); Henthorn et al.,	immune response, and
			Proc Natl Acad Sci USA	suppressing a T cell-mediated
			85:6342-6346 (1988); and	immune response. Additional

highly preferred indications include inflammation and	inflammatory disorders, and	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,
Black et al., Virus Genes 12(2):105-117 (1997), the	content of each of which are	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.															

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				asthma and altergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HNGJT54	739	Production of MCP-1	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An
			activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the	alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly

		invention (including antibodies	preferred indication is
		and agonists or antagonists of	infection (e.g., an infectious
		and agomists of antagomists of the invention) to mediate	disease as described below
		imminomodulation, induce	under "Infectious Disease").
	-	chemotaxis, and modulate	Additional highly preferred
		immune cell activation.	indications include
		Exemplary assays that test for	inflammation and
		immunomodulatory proteins	inflammatory disorders.
 		evaluate the production of cell	Preferred indications include
		surface markers, such as	blood disorders (e.g., as
 		monocyte chemoattractant	described below under
		protein (MCP), and the	"Immune Activity", "Blood-
		activation of monocytes and T	Related Disorders", and/or
		cells. Such assays that may be	"Cardiovascular Disorders").
		used or routinely modified to	Highly preferred indications
		test immunomodulatory and	include autoimmune diseases
		diffferentiation activity of	(e.g., rheumatoid arthritis,
		polypeptides of the invention	systemic lupus erythematosis,
		(including antibodies and	multiple sclerosis and/or as
		agonists or antagonists of the	described below) and
		invention) include assays	immunodeficiencies (e.g., as
		disclosed in Miraglia et al., J	described below). Preferred
		Biomolecular Screening 4:193-	indications also include
 		204(1999); Rowland et al.,	anemia, pancytopenia,
		"Lymphocytes: a practical	leukopenia, thrombocytopenia,
		approach" Chapter 6:138-160	Hodgkin's disease, acute
		(2000); Satthaporn and	lymphocytic anemia (ALL),
		Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
		45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
		Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
		158:2919-2925 (1997), the	disease, inflammatory bowel

			contents of each of which are	disease, sepsis, neutropenia,
			herein incorporated by	neutrophilia, psoriasis,
			reference in its entirety.	suppression of immune
			Human dendritic cells that may	reactions to transplanted
			be used according to these	organs and tissues,
 	_		assays may be isolated using	hemophilia, hypercoagulation,
			techniques disclosed herein or	diabetes mellitus, endocarditis,
			otherwise known in the art.	meningitis (bacterial and
			Human dendritic cells are	viral), Lyme Disease, asthma,
 			antigen presenting cells in	and allergy Preferred
			suspension culture, which,	indications also include
		-	when activated by antigen	neoplastic diseases (e.g.,
			and/or cytokines, initiate and	leukemia, lymphoma, and/or as
			upregulate T cell proliferation	described below under
			and functional activities.	"Hyperproliferative
				Disorders"). Highly preferred
				indications include neoplasms
				and cancers, such as, leukemia,
				lymphoma, prostate, breast,
				lung, colon, pancreatic,
 				esophageal, stomach, brain,
 				liver, and urinary cancer. Other
				preferred indications include
				benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
HNGND37	740	Regulation of	Assays for the regulation of	A highly preferred
		transcription	transcription through the	indication is diabetes mellitus.
		through the PEPCK	PEPCK promoter are well-	An additional highly preferred

		nromoter in	known in the art and may be	indication is a complication
		henatocytes	used or routinely modified to	associated with diabetes (e.g.,
			assess the ability of	diabetic retinopathy, diabetic
_			polypeptides of the invention	nephropathy, kidney disease
			(including antibodies and	(e.g., renal failure,
	_		agonists or antagonists of the	nephropathy and/or other
			invention) to activate the	diseases and disorders as
			PEPCK promoter in a reporter	described in the "Renal
			construct and regulate liver	Disorders" section below),
			gluconeogenesis. Exemplary	diabetic neuropathy, nerve
			assays for regulation of	disease and nerve damage
			transcription through the	(e.g., due to diabetic
	_		PEPCK promoter that may be	neuropathy), blood vessel
			used or routinely modified to	blockage, heart disease, stroke,
			test for PEPCK promoter	impotence (e.g., due to diabetic
			activity (in hepatocytes) of	neuropathy or blood vessel
			polypeptides of the invention	blockage), seizures, mental
			(including antibodies and	confusion, drowsiness,
			agonists or antagonists of the	nonketotic hyperglycemic-
	-		invention) include assays	hyperosmolar coma,
			disclosed in Berger et al., Gene	cardiovascular disease (e.g.,
_			66:1-10 (1998); Cullen and	heart disease, atherosclerosis,
			Malm, Methods in Enzymol	microvascular disease,
			216:362-368 (1992); Henthorn	hypertension, stroke, and other
			et al., Proc Natl Acad Sci USA	diseases and disorders as
			85:6342-6346 (1988);	described in the
			Lochhead et al., Diabetes	"Cardiovascular Disorders"
			49(6):896-903 (2000); and	section below), dyslipidemia,
_			Yeagley et al., J Biol Chem	endocrine disorders (as
			275(23):17814-17820 (2000),	described in the "Endocrine
			the contents of each of which	Disorders" section below),

is herein incorporated by	neuropathy, vision impairment
reference in its entirety.	(e.g., diabetic retinopathy and
Hepatocyte cells that may be	blindness), ulcers and impaired
used according to these assays	wound healing, infection (e.g.,
are publicly available (e.g.,	an infectious diseases or
through the ATCC) and/or	disorders as described in the
may be routinely generated.	"Infectious Diseases" section
Exemplary liver hepatoma	below, especially of the
 cells that may be used	urinary tract and skin), carpal
according to these assays	tunnel syndrome and
include H4lle cells, which	Dupuytren's contracture).
 contain a tyrosine amino	An additional highly preferred
transferase that is inducible	indication is obesity and/or
with glucocorticoids, insulin,	complications associated with
or cAMP derivatives.	obesity. Additional highly
	preferred indications include
	weight loss or alternatively,
	weight gain. Additional
	highly preferred indications are
	complications associated with
	insulin resistance.
	Additional highly preferred
	indications are disorders of the
	musculoskeletal systems
	including myopathies,
	muscular dystrophy, and/or as
	described herein.
	Additional highly preferred
	indications include glycogen
	storage disease (e.g.,
	glycogenoses), hepatitis,

			gallstones, cirrhosis of the
			liver, degenerative or necrotic
			liver disease, alcoholic liver
			diseases, fibrosis, liver
-			regeneration, metabolic
			disease, dyslipidemia and
			cholesterol metabolism, and
			hepatocarcinomas.
			Highly preferred indications
			include blood disorders (e.g.,
			as described below under
			"Immune Activity",
			"Cardiovascular Disorders",
			and/or "Blood-Related
			Disorders"), immune disorders
			(e.g., as described below under
			"Immune Activity"), infection
			(e.g., an infectious disease
			and/or disorder as described
			below under "Infectious
			Disease"), endocrine disorders
_			(e.g., as described below under
			"Endocrine Disorders"), and
			neural disorders (e.g., as
-			described below under "Neural
			Activity and Neurological
		_	Diseases").
			Additional preferred
			indications include neoplastic
			diseases (e.g., as described
			below under

	an influx of calcium, leading to	blockage, heart disease, stroke,
-	activation of calcium	impotence (e.g., due to diabetic
	responsive signaling pathways	neuropathy or blood vessel
	and alterations in cell	blockage), seizures, mental
	functions. Exemplary assays	confusion, drowsiness,
	that may be used or routinely	nonketotic hyperglycemic-
	modified to measure calcium	hyperosmolar coma,
	flux by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Satin LS, et al.,	diseases and disorders as
	Endocrinology, 136(10):4589-	described in the
	601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
	Endocrinology, 136(7):2960-6	section below), dyslipidemia,
	(1995); Richardson SB, et al.,	endocrine disorders (as
	Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
	(1992); and, Meats, JE, et al.,	Disorders" section below),
	Cell Calcium 1989 Nov-	neuropathy, vision impairment
	Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
	contents of each of which is	blindness), ulcers and impaired
	herein incorporated by	wound healing, and infection
	reference in its entirety.	(e.g., infectious diseases and
	Pancreatic cells that may be	disorders as described in the
	used according to these assays	"Infectious Diseases" section
	are publicly available (e.g.,	below, especially of the
	through the ATCC) and/or	urinary tract and skin), carpal
	may be routinely generated.	tunnel syndrome and
	Exemplary pancreatic cells that	Dupuytren's contracture).
	may be used according to these	An additional highly preferred
	assays include HITT15 Cells.	indication is obesity and/or

			HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78:	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
HNGOI12	741	Production of IL-10 and activation of T-cells.	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as

described below), boosting a T cell-mediated immune	response, and suppressing a T	cell-mediated immune	response.																										
polypeptides and antibodies of the invention (including	agonists or antagonists of the	invention) to modulate IL-10	production and/or T-cell	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be	used according to these assays	include Th2 cells. IL10	secreted from Th2 cells may be	measured as a marker of Th2	cell activation. Th2 cells are	a class of T cells that secrete	IL4, IL10, IL13, IL5 and IL6.	Factors that induce	differentiation and activation	of Th2 cells play a major role	in the initiation and
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				pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	
	HNGOM56	742	Activation of transcription through serum response element in	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha
			immune cells (such as T-cells).	art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or	production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha
-				antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related	production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
				genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of	"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies

boosting a T cell-mediated immine response and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,
disclosed in Berger et al., Gene 66.1-10 (1998): Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety.	Human T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the JURKAT	cell line, which is a suspension	culture of leukemia cells that	produce IL-2 when stimulated.									
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			metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia,
			Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple
			myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous
			disease, inflammatory bowel disease, neutropenia,
			suppression of immune
•	•		reactions to transplanted
			organs and tissues,
			diabetes mellitus, endocarditis,
			meningitis, Lyme Disease,
			cardiac reperfusion injury, and
			asthma and allergy. An
			additional preferred indication
			is infection (e.g., an infectious
			disease as described below
	Protection from	Caspase Apoptosis Rescue.	A highly preferred
	Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
	Apoptosis.	rescue are well known in the	includes a method for
		art and may be used or	stimulating endothelial cell
		routinely modified to assess	growth. An alternative highly
		the ability of the polypeptides	preferred embodiment of the
		of the invention (including	invention includes a method

	antibodies and aconists or	for inhibiting endothelial cell
	 antagonists of the invention) to	growth. A highly preferred
	 inhibit caspase protease-	O
	mediated apoptosis.	includes a method for
	Exemplary assays for caspase	stimulating endothelial cell
	 apoptosis that may be used or	proliferation. An alternative
	routinely modified to test	highly preferred embodiment
	caspase apoptosis rescue of	of the invention includes a
	polypeptides of the invention	method for inhibiting
	 (including antibodies and	endothelial cell proliferation.
	 agonists or antagonists of the	A highly preferred
	invention) include the assays	embodiment of the invention
	disclosed in Romeo et al.,	includes a method for
	 Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
	(2000); Messmer et al., Br J	growth. An alternative highly
	 Pharmacol 127(7): 1633-1640	preferred embodiment of the
	(1999); and J Atheroscler	invention includes a method
	Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
	 the contents of each of which	growth. A highly preferred
	 are herein incorporated by	embodiment of the invention
	 reference in its entirety.	includes a method for
	Endothelial cells that may be	stimulating apoptosis of
	used according to these assays	endothelial cells. An
	are publicly available (e.g.,	alternative highly preferred
	 through commercial sources).	embodiment of the invention
	Exemplary endothelial cells	includes a method for
	that may be used according to	inhibiting (e.g., decreasing)
	these assays include bovine	apoptosis of endothelial cells.
	aortic endothelial cells	A highly preferred
	(bAEC), which are an example	embodiment of the invention
	of endothelial cells which line	includes a method for

stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or
blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.			-															-							
					7.	~					·																			

				as describe	as described below under
				"Cardiovas	"Cardiovascular Disorders")
				Caldiova:	Scular Discrincis).
				Highly pre	Highly preferred indications
				include ca	include cardiovascular,
				endothelial	endothelial and/or angiogenic
				disorders (disorders (e.g., systemic
	-			disorders tl	disorders that affect vessels
	-			such as dia	such as diabetes mellitus, as
				well as disc	well as diseases of the vessels
	•		<u> </u>	themselves	themselves, such as of the
_	•			arteries, ca	arteries, capillaries, veins
-	•			and/or lym	and/or lymphatics). Highly
				preferred a	preferred are indications that
				stimulate a	stimulate angiogenesis and/or
_				cardiovasc	cardiovascularization. Highly
				preferred a	preferred are indications that
				inhibit ang	inhibit angiogenesis and/or
	_		•	cardiovasc	cardiovascularization.
				Highly pre	Highly preferred indications
				include ant	include antiangiogenic activity
				to treat solid tumors,	id tumors,
				leukemias,	leukemias, and Kaposi"s
				sarcoma, a	sarcoma, and retinal disorders.
				Highly pre	Highly preferred indications
		-		include nec	include neoplasms and cancer,
				such as, Ka	such as, Kaposi"s sarcoma,
		-	-	hemangion	hemangioma (capillary and
_				cavernous	cavernous), glomus tumors,
				telangiecta	telangiectasia, bacillary
				angiomatosis,	sis,
				hemangioe	hemangioendothelioma,

			angiosarcoma,
			haemangiopericytoma.
			lymphangioma.
			lymphangiosarcoma. Highly
	•		preferred indications also
			include cancers such as,
			prostate, breast, lung, colon,
			pancreatic, esophageal,
-			stomach, brain, liver, and
			urinary cancer. Preferred
			indications include benign
			dysproliferative disorders and
			pre-neoplastic conditions, such
			as, for example, hyperplasia,
			metaplasia, and/or dysplasia.
			Highly preferred indications
	-		also include arterial disease,
			such as, atherosclerosis,
			hypertension, coronary artery
			disease, inflammatory
			vasculitides, Reynaud"s
			disease and Reynaud"s
			phenomenom, aneurysms,
			restenosis; venous and
			lymphatic disorders such as
		_	thrombophlebitis,
	-		lymphangitis, and
			lymphedema; and other
	-		vascular disorders such as
			'asc
	•		and cancer. Highly

			nreferred indications also
			include trauma such as
			wounds, burns, and injured
	_		tissue (e.g., vascular injury
			such as, injury resulting from
			balloon angioplasty, and
			atheroschlerotic lesions),
	-		implant fixation, scarring,
			ischemia reperfusion injury,
-			rheumatoid arthritis,
	_		cerebrovascular disease, renal
			diseases such as acute renal
			failure, and osteoporosis.
	-	-	Additional highly preferred
			indications include stroke,
	-		graft rejection, diabetic or
			other retinopathies, thrombotic
			and coagulative disorders,
			vascularitis, lymph
			angiogenesis, sexual disorders,
		_	age-related macular
			degeneration, and treatment
			/prevention of endometriosis
			and related conditions.
			Additional highly preferred
			indications include fibromas,
-			heart disease, cardiac arrest,
			heart valve disease, and
			vascular disease. Preferred
	-		indications include blood
			disorders (e.g., as described

					below under "Immune
					Activity", "Blood-Related
					Disorders", and/or
····					"Cardiovascular Disorders").
-					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
		,			inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HNGOW62	744	Protection from	Caspase Apoptosis Rescue.	A highly preferred
			Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
			Apoptosis.	rescue are well known in the	includes a method for
				art and may be used or	stimulating endothelial cell
			-	routinely modified to assess	growth. An alternative highly
				the ability of the polypeptides	preferred embodiment of the
				of the invention (including	invention includes a method
				antibodies and agonists or	for inhibiting endothelial cell
				antagonists of the invention) to	growth. A highly preferred
				inhibit caspase protease-	embodiment of the invention
				mediated apoptosis.	includes a method for

stimulating endothelial cell proliferation. An alternative highly preferred embodiment	of the invention includes a method for inhibiting endothelial cell proliferation.	A highly preferred embodiment of the invention includes a method for	stimulating endothelial cell crowth. An alternative highly	preferred embodiment of the	invention includes a method for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	unhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for
Exemplary assays for caspase apoptosis that may be used or routinely modified to test	caspase apoptosis rescue of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include the assays	Cardiovasc Res 45(3): 788-794 (2000): Messmer et al. Br. I	Pharmacol 127(7): 1633-1640	(1999); and J Atheroscler Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular
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	permeability, vascular tone.	inhibiting angiogenesis. A
	and immune cell extravasation.	men
		of the invention includes a
		method for reducing cardiac
		hypertrophy. An alternative
		highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as
		described below under
		"Hyperproliferative
		Disorders"), and disorders of
		the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
		aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
-		dysfunction, atherosclerosis
		and atherosclerotic vascular
		disease, diabetic nephropathy,
		intracardiac shunt, cardiac
		hypertrophy, myocardial
		infarction, chronic
		hemodynamic overload, and/or
		as described below under
	-	"Cardiovascular Disorders").
		Highly preferred indications
		include cardiovascular,

			endothelial and/or angiogenic
			disorders (e.g., systemic
			disorders that affect vessels
			such as diabetes mellitus, as
	•		well as diseases of the vessels
			themselves, such as of the
			arteries, capillaries, veins
_			and/or lymphatics). Highly
			preferred are indications that
			stimulate angiogenesis and/or
			cardiovascularization. Highly
			preferred are indications that
			inhibit angiogenesis and/or
			cardiovascularization.
			Highly preferred indications
			include antiangiogenic activity
			to treat solid tumors,
			leukemias, and Kaposi"s
			sarcoma, and retinal disorders.
			Highly preferred indications
			include neoplasms and cancer,
			such as, Kaposi"s sarcoma,
			hemangioma (capillary and
			cavernous), glomus tumors,
			telangiectasia, bacillary
			angiomatosis,
			hemangioendothelioma,
			angiosarcoma,
			haemangiopericytoma,
			Iymphangioma,
			lymphangiosarcoma. Highly

			preferred indications also
 			include cancers such as.
 			prostate, breast, lung, colon,
			pancreatic, esophageal,
			stomach, brain, liver, and
	 -		urinary cancer. Preferred
			indications include benign
			dysproliferative disorders and
			pre-neoplastic conditions, such
 			as, for example, hyperplasia,
 			metaplasia, and/or dysplasia.
			Highly preferred indications
			also include arterial disease,
			such as, atherosclerosis,
 			hypertension, coronary artery
			disease, inflammatory
	-		vasculitides, Reynaud"s
			disease and Reynaud"s
			phenomenom, aneurysms,
<u> </u>	•		restenosis; venous and
			lymphatic disorders such as
 			thrombophlebitis,
 			lymphangitis, and
 			lymphedema; and other
 			vascular disorders such as
 			peripheral vascular disease,
 	-		and cancer. Highly
			preferred indications also
 			include trauma such as
 			wounds, burns, and injured
			tissue (e.g., vascular injury

				Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
нинеп93	745	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders, immunological disorders, ienmunological disorders, cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders",

			vessels, and are involved in	"Hyperproliferative Disorders"
			functions that include, but are	and/or "Cardiovascular
			not limited to, angiogenesis,	Disorders"). Highly preferred
			vascular permeability, vascular	indications include neoplasms
			tone, and immune cell	and cancers such as, for
			extravasation. Exemplary	example, leukemia, lymphoma,
			endothelial cells that may be	melanoma, renal cell
			used according to these assays	carcinoma, and prostate,
			include human umbilical vein	breast, lung, colon, pancreatic,
			endothelial cells (HUVEC),	esophageal, stomach, brain,
			which are available from	liver and urinary cancer. Other
			commercial sources. The	preferred indications include
			expression of VCAM	benign dysproliferative
			(CD106), a membrane-	disorders and pre-neoplastic
			associated protein, can be	conditions, such as, for
			upregulated by cytokines or	example, hyperplasia,
			other factors, and contributes	metaplasia, and/or dysplasia.
			to the extravasation of	
			lymphocytes, leucocytes and	
			other immune cells from blood	
			vessels; thus VCAM	
			expression plays a role in	
			promoting immune and	
			inflammatory responses.	
HNHEU93	745	Stimulation of	Assays for measuring secretion	A highly preferred
		insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
		from pancreatic	the art and may be used or	An additional highly preferred
		beta cells.	routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease

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(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing and infection
antagonists of the invention) to	sumulate insulin secretion.	For example, insulin secretion	is measured by FMAT using	anti-rat insulin antibodies.	Insulin secretion from	pancreatic beta cells is	upregulated by glucose and	also by certain	proteins/peptides, and	disregulation is a key	component in diabetes.	Exemplary assays that may be	used or routinely modified to	test for stimulation of insulin	secretion (from pancreatic	cells) by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Ahren, B., et al.,	Am J Physiol, 277(4 Pt	2):R959-66 (1999); Li, M., et	al., Endocrinology,	138(9):3735-40 (1997); Kim,	K.H., et al., FEBS Lett,	377(2):237-9 (1995); and,	Miraglia S et. al., Journal of	Biomolecular Screening,	4:193-204 (1999), the contents	of each of which is herein
				-																										
																														_
													-																	

			incorporated by reference in its entirety. Pancreatic cells that	(e.g., infectious diseases and disorders as described in the
			may be used according to these	"Infectious Diseases" section
			assays are publicly available	below, especially of the
			(e.g., through the ATCC)	urinary tract and skin), carpal
			and/or may be routinely	tunnel syndrome and
			generated. Exemplary	Dupuytren's contracture).
			pancreatic cells that may be	An additional highly preferred
			used according to these assays	indication is obesity and/or
			include rat INS-1 cells. INS-1	complications associated with
			cells are a semi-adherent cell	obesity. Additional highly
			line established from cells	preferred indications include
			isolated from an X-ray induced	weight loss or alternatively,
			rat transplantable insulinoma.	weight gain. Aditional
			These cells retain	highly preferred indications are
			characteristics typical of native	complications associated with
			pancreatic beta cells including	insulin resistance.
			glucose inducible insulin	
			secretion. References: Asfari	
			et al. Endocrinology 1992	
			130:167.	
 HNHFM14	746	Inhibition of	Reporter Assay: construct	
		squalene synthetase	contains regulatory and coding	
		gene transcription.	sequence of squalene	
			synthetase, the first specific	
			enzyme in the cholesterol	
			biosynthetic pathway. See	
			Jiang, et al., J. Biol. Chem.	
			268:12818-128241(993), the	
			contents of which are herein	
			incorporated by reference in its	

-				entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its	
				entirety.	
HNH	HNHFM14	746	Stimulation of	Assays for measuring calcium	A highly preferred
			Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
			pancreatic beta	and may be used or routinely	An additional highly preferred
vi e			cells.	modified to assess the ability	indication is a complication
				of polypeptides of the	associated with diabetes (e.g.,
-				invention (including antibodies	diabetic retinopathy, diabetic
				and agonists or antagonists of	nephropathy, kidney disease
				the invention) to mobilize	(e.g., renal failure,
				calcium. For example, the	nephropathy and/or other
				FLPR assay may be used to	diseases and disorders as
				measure influx of calcium.	described in the "Renal
-				Cells normally have very low	Disorders" section below),
				concentrations of cytosolic	diabetic neuropathy, nerve
	-			calcium compared to much	disease and nerve damage
				higher extracellular calcium.	(e.g., due to diabetic
				Extracellular factors can cause	neuropathy), blood vessel
				an influx of calcium, leading to	blockage, heart disease, stroke,
				activation of calcium	impotence (e.g., due to diabetic
				responsive signaling pathways	neuropathy or blood vessel
				and alterations in cell	blockage), seizures, mental

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confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g.,	heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as	described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as	described in the "Endocrine	Disorders" section below),	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal				indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	waight lose or alternatively
functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the	invention (including antibodies and agonists or antagonists of	the invention) include assays disclosed in: Satin LS, et al.,	Endocrinology, 136(10):4589- 601 (1995);Mogami H, et al.,	Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al.,	Biochem J, 288 (Pt 3):847-51	(1992); and, Meats, JE, et al., Cell Calcium 1989 Nov-	Dec;10(8):535-41 (1989), the	contents of each of which is	herein incorporated by	reference in its entirety. Pancreatic cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary pancreatic cells that	may be used according to these	assays include HITT15 Cells.	HITT15 are an adherent	epithelial cell line established	from Syrian hamster islet cells	transformed with SV40 These
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			cells express glucagon, somatostatin, and glucocorticoid receptors. The	weight gain. Aditional highly preferred indications are complications associated with
			cells secrete insulin, which is	insulin resistance.
			sumulated by glucose and glucagon and suppressed by	
			somatostatin or	
			glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
			4339-4343, 1981.	
HNHNB29	748	Regulation of	Assays for the regulation of	A highly preferred
		transcription	transcription through the	indication is diabetes mellitus.
		through the PEPCK	PEPCK promoter are well-	An additional highly preferred
		promoter in	known in the art and may be	indication is a complication
		hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
			assess the ability of	diabetic retinopathy, diabetic
			polypeptides of the invention	nephropathy, kidney disease
			(including antibodies and	(e.g., renal failure,
			agonists or antagonists of the	nephropathy and/or other
			invention) to activate the	diseases and disorders as
			PEPCK promoter in a reporter	described in the "Renal
			construct and regulate liver	Disorders" section below),
			gluconeogenesis. Exemplary	diabetic neuropathy, nerve
			assays for regulation of	disease and nerve damage
			transcription through the	(e.g., due to diabetic
			PEPCK promoter that may be	neuropathy), blood vessel
			used or routinely modified to	blockage, heart disease, stroke,
			test for PEPCK promoter	impotence (e.g., due to diabetic

		activity (in hepatocytes) of	neuropathy or blood vessel
		polypeptides of the invention	blockage), seizures, mental
		(including antibodies and	confusion, drowsiness,
		agonists or antagonists of the	nonketotic hyperglycemic-
		invention) include assays	hyperosmolar coma,
		disclosed in Berger et al., Gene	cardiovascular disease (e.g.,
		66:1-10 (1998); Cullen and	heart disease, atherosclerosis,
		Malm, Methods in Enzymol	microvascular disease,
		216:362-368 (1992); Henthorn	hypertension, stroke, and other
		et al., Proc Natl Acad Sci USA	diseases and disorders as
		85:6342-6346 (1988);	described in the
		Lochhead et al., Diabetes	"Cardiovascular Disorders"
		49(6):896-903 (2000); and	section below), dyslipidemia,
		Yeagley et al., J Biol Chem	endocrine disorders (as
		275(23):17814-17820 (2000),	described in the "Endocrine
		the contents of each of which	Disorders" section below),
	-	is herein incorporated by	neuropathy, vision impairment
		reference in its entirety.	(e.g., diabetic retinopathy and
		Hepatocyte cells that may be	blindness), ulcers and impaired
		used according to these assays	wound healing, infection (e.g.,
		are publicly available (e.g.,	an infectious diseases or
		through the ATCC) and/or	disorders as described in the
		may be routinely generated.	"Infectious Diseases" section
	-	Exemplary liver hepatoma	below, especially of the
		cells that may be used	urinary tract and skin), carpal
		according to these assays	tunnel syndrome and
		include H4lle cells, which	Dupuytren's contracture).
		contain a tyrosine amino	An additional highly preferred
		transferase that is inducible	indication is obesity and/or
		with glucocorticoids, insulin,	complications associated with
		or cAMP derivatives.	obesity. Additional highly

weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with	Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies,	described herein. Additional highly preferred indications include glycogen storage disease (e.g., glycogenoses), hepatitis, gallstones, cirrhosis of the	liver, degenerative or necrotic liver disease, alcoholic liver diseases, fibrosis, liver regeneration, metabolic disease, dyslipidemia and cholesterol metabolism, and	hepatocarcinomas. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related

		(e o as described below under
		III
		"Immune Activity"), infection
_		(e.g., an infectious disease
		and/or disorder as described
		below under "Infectious
		Disease"), endocrine disorders
		(e.g., as described below under
		"Endocrine Disorders"), and
		neural disorders (e.g., as
	-	described below under "Neural
		Activity and Neurological
		Diseases").
		Additional preferred
		indications include neoplastic
		diseases (e.g., as described
		below under
		"Hyperproliferative
		Disorders"). Preferred
		indications include neoplasms
	•	and cancers, such as, leukemia,
		lymphoma, prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
`		and urinary cancer. A highly
		preferred indication is liver
		cancer. Other preferred
		indications include benign
_		dysproliferative disorders and
		pre-neoplastic conditions, such
		as, for example, hyperplasia,
		metaplasia, and/or dysplasia.

	HNHOD46	749	SEAP in 293/ISRE		
	HNHOD46	749	Activation of	Kinase assay. Kinase assays,	A highly preferred
			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
				inhibit cell proliferation,	adipocyte differentiation. An
				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
				kinase activity that may be	includes a method for
				used or routinely modified to	inhibiting adipocyte
			-	test ERK kinase-induced	differentiation. A highly
				activity of polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method
				and agonists or antagonists of	for stimulating (e.g.,
				the invention) include the	increasing) adipocyte
				assays disclosed in Forrer et	activation. An alternative
				al., Biol Chem 379(8-9):1101-	highly preferred embodiment
				1110 (1998); Le Marchand-	of the invention includes a
				Brustel Y, Exp Clin	method for inhibiting the
				Endocrinol Diabetes	activation of (e.g., decreasing)
				107(2):126-132 (1999);	and/or inactivating adipocytes.
-				Kyriakis JM, Biochem Soc	Highly preferred indications
				Symp 64:29-48 (1999); Chang	include endocrine disorders

		and Karin, Nature	(e.g., as described below under
		410(6824):37-40 (2001); and	"Endocrine Disorders").
		Cobb MH, Prog Biophys Mol	Highly preferred indications
		Biol 71(3-4):479-500 (1999);	also include neoplastic
		the contents of each of which	diseases (e.g., lipomas,
		are herein incorporated by	liposarcomas, and/or as
		reference in its entirety.	described below under
		Mouse adipocyte cells that	"Hyperproliferative
		may be used according to these	Disorders"). Preferred
		assays are publicly available	indications include blood
		(e.g., through the ATCC).	disorders (e.g., hypertension,
		Exemplary mouse adipocyte	congestive heart failure, blood
		cells that may be used	vessel blockage, heart disease,
		according to these assays	stroke, impotence and/or as
		include 3T3-L1 cells. 3T3-L1	described below under
	-	is an adherent mouse	"Immune Activity",
	-	preadipocyte cell line that is a	"Cardiovascular Disorders",
		continuous substrain of 3T3	and/or "Blood-Related
		fibroblast cells developed	Disorders"), immune disorders
		through clonal isolation and	(e.g., as described below under
•		undergo a pre-adipocyte to	"Immune Activity"), neural
		adipose-like conversion under	disorders (e.g., as described
		appropriate differentiation	below under "Neural Activity
	-	conditions known in the art.	and Neurological Diseases"),
			and infection (e.g., as
			described below under
			"Infectious Disease").
			A highly preferred indication
			is diabetes mellitus. An
			additional highly preferred
			indication is a complication

	associated with diabetes (e.g.
	diabetic retinopathy, diabetic
	nephropathy, kidney disease
	(e.g., renal failure,
	nephropathy and/or other
	diseases and disorders as
	described in the "Renal
	Disorders" section below),
 	diabetic neuropathy, nerve
	disease and nerve damage
	(e.g., due to diabetic
	neuropathy), blood vessel
	blockage, heart disease, stroke,
	impotence (e.g., due to diabetic
	neuropathy or blood vessel
	blockage), seizures, mental
	confusion, drowsiness,
	nonketotic hyperglycemic-
	hyperosmolar coma,
	cardiovascular disease (e.g.,
	heart disease, atherosclerosis,
 	microvascular disease,
	hypertension, stroke, and other
	diseases and disorders as
 	described in the
	"Cardiovascular Disorders"
	section below), dyslipidemia,
 	endocrine disorders (as
	described in the "Endocrine
	Disorders" section below),
-	neuropathy, vision impairment

(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	
																												-	

				, di
				disorders. Preferred
				indications include neoplasms
				and cancer, such as,
				lymphoma, leukemia and
				breast, colon, and kidney
				cancer. Additional preferred
				indications include melanoma,
	-			prostate, lung, pancreatic,
				esophageal, stomach, brain,
				liver, and urinary cancer.
				Highly preferred indications
				include lipomas and
				liposarcomas. Other preferred
				indications include benign
				dysproliferative disorders and
				pre-neoplastic conditions, such
-				as, for example, hyperplasia,
				metaplasia, and/or dysplasia.
HNHOD46	749	Regulation of	Assays for the regulation of	A highly preferred indication
		transcription via	transcription through the	is diabetes mellitus.
		DMEF1 response	DMEF1 response element are	Additional highly preferred
		element in	well-known in the art and may	indications include
		adipocytes and pre-	be used or routinely modified	complications associated with
		adipocytes	to assess the ability of	diabetes (e.g., diabetic
			polypeptides of the invention	retinopathy, diabetic
			(including antibodies and	nephropathy, kidney disease
			agonists or antagonists of the	(e.g., renal failure,
			invention) to activate the	nephropathy and/or other
			DMEF1 response element in a	diseases and disorders as
			reporter construct (such as that	described in the "Renal

Disorders" section below), diabetic neuropathy, nerve	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic		blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the
containing the GLUT4 promoter) and to regulate	DMEF1 response element is	present in the GLUT4	promoter and binds to MEF2 transcription factor and another	transcription factor that is	required for insulin regulation	of Glut4 expression in skeletal	muscle. GLUT4 is the primary	insulin-responsive glucose	transporter in fat and muscle	tissue. Exemplary assays that	may be used or routinely	modified to test for DMEF1	response element activity (in	adipocytes and pre-adipocytes)	by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Thai, M.V., et al., J	Biol Chem, 273(23):14285-92	(1998); Mora, S., et al., J Biol	Chem, 275(21):16323-8	(2000); Liu, M.L., et al., J Biol	Chem, 269(45):28514-21	(1994); "Identification of a 30-	base pair regulatory element	and novel DNA binding

			protein that regulates the	urinary tract and skin). An
			human GLUT4 promoter in	additional highly preferred
			transgenic mice", J Biol Chem.	indication is obesity and/or
			2000 Aug 4;275(31):23666-73;	complications associated with
			Berger, et al., Gene 66:1-10	obesity. Additional highly
			(1988); and, Cullen, B., et al.,	preferred indications include
-			Methods in Enzymol.	weight loss or alternatively,
			216:362–368 (1992), the	weight gain. Additional highly
			contents of each of which is	preferred indications are
-			herein incorporated by	complications associated with
_			reference in its entirety.	insulin resistance.
			Adipocytes and pre-adipocytes	
			that may be used according to	-
-			these assays are publicly	
			available (e.g., through the	
			ATCC) and/or may be	
			routinely generated.	
			Exemplary cells that may be	
			used according to these assays	
			include the mouse 3T3-L1 cell	
			line which is an adherent	
			mouse preadipocyte cell line.	
			Mouse 3T3-L1 cells are a	
			continuous substrain of 3T3	
			fibroblasts developed through	
			clonal isolation. These cells	
			undergo a pre-adipocyte to	
			adipose-like conversion under	
			appropriate differentiation	
	, , , , , , , , , , , , , , , , , , , ,		culture conditions.	
HNHOD46	749	Activation of	Assays for the activation of	A highly preferred indication

	transcription	transcription through the	is obesity and/or complications
	through cAMP	cAMP response element are	associated with obesity.
	response element	well-known in the art and may	Additional highly preferred
	(CRE) in pre-	be used or routinely modified	indications include weight loss
	adipocytes.	to assess the ability of	or alternatively, weight gain.
		polypeptides of the invention	An additional highly preferred
		(including antibodies and	indication is diabetes mellitus.
		agonists or antagonists of the	An additional highly preferred
		invention) to increase cAMP,	indication is a complication
		regulate CREB transcription	associated with diabetes (e.g.,
		factors, and modulate	diabetic retinopathy, diabetic
		expression of genes involved	nephropathy, kidney disease
		in a wide variety of cell	(e.g., renal failure,
		functions. For example, a	nephropathy and/or other
		3T3-L1/CRE reporter assay	diseases and disorders as
		may be used to identify factors	described in the "Renal
		that activate the cAMP	Disorders" section below),
		signaling pathway. CREB	diabetic neuropathy, nerve
		plays a major role in	disease and nerve damage
_		adipogenesis, and is involved	(e.g., due to diabetic
		in differentiation into	neuropathy), blood vessel
		adipocytes. CRE contains the	blockage, heart disease, stroke,
		binding sequence for the	impotence (e.g., due to diabetic
		transcription factor CREB	neuropathy or blood vessel
		(CRE binding protein).	blockage), seizures, mental
	-	Exemplary assays for	confusion, drowsiness,
		transcription through the	nonketotic hyperglycemic-
		cAMP response element that	hyperosmolar coma,
		may be used or routinely	cardiovascular disease (e.g.,
		modified to test cAMP-	heart disease, atherosclerosis,
		response element activity of	microvascular disease,

		_																												
hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	Additional highly preferred	indications are complications	associated with insulin	resistance.								
polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch	et al., Mol Cell Biol	20(3):1008-1020 (2000); and	Klemm et al., J Biol Chem	273:917-923 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and
									-						-															

			undergo a pre-adipocyte to adipose-like conversion under	
			appropriate differentiation conditions known in the art.	
HNHOD46	749	Activation of	Assays for the activation of	A highly preferred indication
		transcription	transcription through the	is obesity and/or complications
		through serum	Serum Response Element	associated with obesity.
		response element in	(SRE) are well-known in the	Additional highly preferred
		pre-adipocytes.	art and may be used or	indications include weight loss
			routinely modified to assess	or alternatively, weight gain.
			the ability of polypeptides of	An additional highly preferred
			the invention (including	indication is diabetes mellitus.
			antibodies and agonists or	An additional highly preferred
			antagonists of the invention) to	indication is a complication
			regulate the serum response	associated with diabetes (e.g.,
			factors and modulate the	diabetic retinopathy, diabetic
			expression of genes involved	nephropathy, kidney disease
			in growth. Exemplary assays	(e.g., renal failure,
			for transcription through the	nephropathy and/or other
			SRE that may be used or	diseases and disorders as
			routinely modified to test SRE	described in the "Renal
			activity of the polypeptides of	Disorders" section below),
			the invention (including	diabetic neuropathy, nerve
			antibodies and agonists or	disease and nerve damage
			antagonists of the invention)	(e.g., due to diabetic
			include assays disclosed in	neuropathy), blood vessel
		-	Berger et al., Gene 66:1-10	blockage, heart disease, stroke,
			(1998); Cullen and Malm,	impotence (e.g., due to diabetic
			Methods in Enzymol 216:362-	neuropathy or blood vessel
			368 (1992); Henthorn et al.,	blockage), seizures, mental
			Proc Natl Acad Sci USA	confusion, drowsiness,

				85:6342-6346 (1988); and	nonketotic hyperglycemic-
				Black et al., Virus Genes	hyperosmolar coma,
				12(2):105-117 (1997), the	cardiovascular disease (e.g.,
				content of each of which are	heart disease, atherosclerosis,
				herein incorporated by	microvascular disease,
				reference in its entirety. Pre-	hypertension, stroke, and other
				adipocytes that may be used	diseases and disorders as
				according to these assays are	described in the
				publicly available (e.g.,	"Cardiovascular Disorders"
				through the ATCC) and/or	section below), dyslipidemia,
				may be routinely generated.	endocrine disorders (as
				Exemplary mouse adipocyte	described in the "Endocrine
				cells that may be used	Disorders" section below),
				according to these assays	neuropathy, vision impairment
				include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
				is an adherent mouse	blindness), ulcers and impaired
				preadipocyte cell line that is a	wound healing, and infection
				continuous substrain of 3T3	(e.g., infectious diseases and
				fibroblast cells developed	disorders as described in the
				through clonal isolation and	"Infectious Diseases" section
				undergo a pre-adipocyte to	below). Additional highly
				adipose-like conversion under	preferred indications are
				appropriate differentiation	complications associated with
				conditions known in the art.	insulin resistance.
	HNHOD46	749	Activation of	Assays for the activation of	Preferred indications include
			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
8			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an

						
infectious disease as described below under "Infectious Disease"). Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple solerosis and/or as described	below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and	inflammatory disorders. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below	under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma	(e.g., T cell lymphoma, Burkitt's lymphoma, non- Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate,
(including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB	transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary	assays for transcription through the cAMP response element that may be used or routinely modified to test	cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665	(1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are

	c.b.;			may be used according to these preferred indications include				ls. example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease, and	asthma and allergy.		rough the the invention includes a	se Element method for inhibiting (e.g.,	 med or handuction An alternative
101:0:30 :10:17:00	puoliciy avallat	through the A1	Exemplary mor	may be used ac	assays include 1	line, which is a	culture of IL-2 dependent	cytotoxic T cells.																			Activation of Assays for the activation of	ranscription transcription through the	hrough serum Serum Response Element	 immune cells (such art and may be used or

	as T-cells).	routinely modified to assess	preferred embodiment of the
		the ability of polypeptides of	invention includes a method
		the invention (including	for stimulating (e.g.,
		antibodies and agonists or	increasing) TNF alpha
-		antagonists of the invention) to	production. Preferred
		regulate the serum response	indications include blood
		factors and modulate the	disorders (e.g., as described
		expression of genes involved	below under "Immune
		in growth. Exemplary assays	Activity", "Blood-Related
		for transcription through the	Disorders", and/or
		SRE that may be used or	"Cardiovascular Disorders"),
	***	routinely modified to test SRE	Highly preferred indications
	-	activity of the polypeptides of	include autoimmune diseases
		the invention (including	(e.g., rheumatoid arthritis,
		antibodies and agonists or	systemic lupus erythematosis,
		antagonists of the invention)	Crohn"s disease, multiple
		include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and	immune response. Additional
_		Black et al., Virus Genes	highly preferred indications
		12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
		herein incorporated by	treating joint damage in
	-	reference in its entirety. T	patients with rheumatoid
		cells that may be used	arthritis. An additional highly
		according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications

include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,
through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.										-				·			-		-				
																	-													

					neutrophilia, psoriasis,
-					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
-					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HNHOD46	749	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
_				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),

	"Lymphocytes: a practical	indications include neonlasms
	approach" Chapter 6:138-160	and cancers such as myeloma
	approach Chapter 0.130-100	allo calicers, such as, illyeronna,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
-	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.
-	antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,
	when activated by antigen	leukopenia, thrombocytopenia,
	and/or cytokines, initiate and	Hodgkin's disease, acute
	upregulate T cell proliferation	lymphocytic anemia (ALL),
	and functional activities.	multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,
		granulomatous disease,
		inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
		meningitis, and Lyme Disease.
		An additonal preferred

					indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
NH	HNHOD46	749	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory	A highly preferred embodiment of the invention
			•	proteins produced by activated	includes a method for
				dendritic cells that upregulate	stimulating MIP1a production.
				monocyte/macrophage and T	An alternative highly preferred
				cell chemotaxis are well	embodiment of the invention
	•			known in the art and may be	includes a method for
				used or routinely modified to	uci
				assess the ability of	MIP1a production. A highly
				polypeptides of the invention	preferred indication is
				(including antibodies and	infection (e.g., an infectious
				agonists or antagonists of the	disease as described below
				invention) to mediate	under "Infectious Disease").
				immunomodulation, modulate	Preferred indications include
				chemotaxis, and modulate T	blood disorders (e.g., as
				cell differentiation. Exemplary	described below under
				assays that test for	"Immune Activity", "Blood-
				immunomodulatory proteins	Related Disorders", and/or
	-			evaluate the production of	"Cardiovascular Disorders").
				chemokines, such as	Highly preferred indications
				macrophage inflammatory	include autoimmune diseases
				protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
				the activation of	systemic lupus erythematosis,
				monocytes/macrophages and T	multiple sclerosis and/or as
				cells. Such assays that may be	described below) and
			-	used or routinely modified to	immunodeficiencies (e.g., as
				test immunomodulatory and	described below). Additional

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highly preferred indications	include minamination and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma, and allergy.	Preferred indications also	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung. colon. pancreatic.
chemotaxis activity of	polypeptides of tife invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-	29 (2000); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and
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			upregulate T cell proliferation and functional activities.	esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for
HNHOD46	749	SEAP in HIB/CRE		example, hyperplasia, metaplasia, and/or dysplasia.
HNHOD46	749	Activation of transcription	This reporter assay measures activation of the GATA-3	Highly preferred indications include allergy, asthma, and
		through GATA-3 response element in	signaling pathway in HMC-1 human mast cell line.	rhinitis. Additional preferred indications include infection
		immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
		as mast extra).	cytokine and chemokine	"Infectious Disease"), and
		-	production. Assays for the	inflammation and
			activation of transcription	inflammatory disorders.
			through the GATA3 response	Preferred indications also
			element are well-known in the	include blood disorders (e.g.,
			art and may be used or routinely modified to assess	"Immune Activity", "Blood-
			the ability of polypeptides of	Related Disorders", and/or
			the invention (including	"Cardiovascular Disorders").
			antibodies and agonists or	Preferred indications include
			antagonists of the invention) to	autoimmune diseases (e.g.,
			regulate GATA3 transcription	rheumatoid arthritis, systemic
			factors and modulate	lupus erythematosis, multiple
			expression of mast cell genes	sclerosis and/or as described
			important for immune response	below) and
			development. Exemplary	immunodeficiencies (e.g., as

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described below). Preferred indications include neoplastic	diseases (e.g., leukemia, lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,
assays for transcription through the GATA3 response	element that may be used or routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells
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				that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of	hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
	2) dolliar	140	Q	immature mast cells.	
	HNHOD46	749	Activation of transcription	This reporter assay measures activation of the NFAT	Highly preferred indications include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			as mast cells).	Activation of INFA1 in mast cells has been linked to	(e.g., an infectious disease as described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
,				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as

immunomodulatory functions.	described below). Preferred
Exemplary assays for	indications include neoplastic
transcription through the	diseases (e.g., Ieukemia,
NFAT response element that	Iymphoma, melanoma,
may be used or routinely	prostate, breast, lung, colon,
modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
 (including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
85:6342-6346 (1988); De Boer	Preferred indications include
et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
 et al., J Immunol	leukemias, Hodgkin's disease,
165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
al., J Exp Med 188:527-537	granulomatous disease,
(1998), the contents of each of	inflammatory bowel disease,
which are herein incorporated	sepsis, neutropenia,
by reference in its entirety.	neutrophilia, psoriasis,
Mast cells that may be used	suppression of immune
according to these assays are	reactions to transplanted
publicly available (e.g.,	organs and tissues, hemophilia,

hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	
through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	749
	HNHOD46

			present which signals the presence of metabolically	
			active cells. 3T3-L1 is a	
			mouse preadipocyte cell line. It	
		,	is a continuous substrain of	
			3T3 fibroblast cells developed	
			through clonal isolation. Cells	
			were differentiated to an	
			adipose-like state before being	
			used in the screen. See Green	
			H and Meuth M., Cell 3: 127-	
			133 (1974), which is herein	
			incorporated by reference in its	
			entirety.	
HNHOD46	749	IL-10 in Human T-		
		cell 2B9		
HNHOD46	749	SEAP in Jurkat-		
		AP1		
HNHOD46	749	Activation of	Assays for the activation of	Preferred indications include
		transcription	transcription through the	blood disorders (e.g., as
		through cAMP	cAMP response element are	described below under
	٠	response element in	well-known in the art and may	"Immune Activity", "Blood-
		immune cells (such	be used or routinely modified	Related Disorders", and/or
		as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
			polypeptides of the invention	and infection (e.g., an
			(including antibodies and	infectious disease as described
			agonists or antagonists of the	below under "Infectious
			invention) to increase cAMP,	Disease"). Preferred
			bind to CREB transcription	indications include
			factor, and modulate	autoimmune diseases (e.g.,
			expression of genes involved	rheumatoid arthritis, systemic

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lupus erythematosis, multiple	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma (e.g., T cell	lymphoma, Burkitt's	lymphoma, non-Hodgkins	lymphoma, Hodgkin''s	disease), melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such
in a wide variety of cell functions Exemplary assays	for transcription through the	cAMP response element that	may be used or routinely	modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Genes 15(2):105-117	(1997); and Belkowski et al., J	Immunol 161(2):659-665	(1998), the contents of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the JURKAT	cell line, which is a suspension
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				culture of leukemia cells that produce IL-2 when stimulated.	as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include
					anemia, pancytopenia,
					acute lymphocytic anemia
-					(ALL), plasmacytomas,
					AIDS. granulomatous disease.
	_				inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HNHOD46	749	Activation of	Assays for the activation of	Highly preferred indications
•			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response in immune	cells (NFAT) response element	"Immune Activity", "Blood-
			cells (such as T-	are well-known in the art and	Related Disorders", and/or
	_		cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),

	modulate expression of genes	immunodeficiencies (e.g., as
	involved in	described below), boosting a T
	immunomodulatory functions.	cell-mediated immune
	Exemplary assays for	response, and suppressing a T
	transcription through the	cell-mediated immune
	NFAT response element that	response. Additional highly
	may be used or routinely	preferred indications include
	modified to test NFAT-	inflammation and
	response element activity of	inflammatory disorders. An
 	polypeptides of the invention	additional highly preferred
 	(including antibodies and	indication is infection (e.g., an
	agonists or antagonists of the	infectious disease as described
	invention) include assays	below under "Infectious
	disclosed in Berger et al., Gene	Disease"). Preferred
 	66:1-10 (1998); Cullen and	indications include neoplastic
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
 	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988); Serfling	"Hyperproliferative
	et al., Biochim Biophys Acta	Disorders"). Preferred
	1498(1):1-18 (2000); De Boer	indications include neoplasms
	et al., Int J Biochem Cell Biol	and cancers, such as, for
	31(10):1221-1236 (1999);	example, leukemia, lymphoma,
 _	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. T	pre-neoplastic conditions, such
	cells that may be used	as, for example, hyperplasia,

				according to these assays are publicly available (e.g.,	metaplasia, and/or dysplasia. Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human T cells that	leukopenia, thrombocytopenia,
				may be used according to these	Hodgkin's disease, acute
				assays include the JURKAT	lymphocytic anemia (ALL),
				cell line, which is a suspension	plasmacytomas, multiple
				culture of leukemia cells that	myeloma, Burkitt's lymphoma,
				produce IL-2 when stimulated.	arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
	-				organs and tissues,
·-					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HNHOD46	749	Activation of	This reporter assay measures	Highly preferred indication
			transcription	activation of the NFkB	includes allergy, asthma, and
			through NFKB	signaling pathway in Ku812	rhinitis. Additional highly
			response element in	human basophil cell line.	preferred indications include
	-		immune cells (such	Assays for the activation of	infection (e.g., an infectious
			as basophils).	transcription through the	disease as described below
				NFKB response element are	under "Infectious Disease"),
				well-known in the art and may	and inflammation and
				be used or routinely modified	inflammatory disorders.
				to assess the ability of	Preferred indications include
			-	polypeptides of the invention	immunological and
				(including antibodies and	hempatopoietic disorders (e.g.,

		agonists or antagonists of the	as described below under
		invention) to regulate NFKB	"Immine Activity", and
		transcription factors and	"Blood-Related Disorders").
		modulate expression of	Preferred indications also
		immunomodulatory genes.	include autoimmune diseases
		Exemplary assays for	(e.g., rheumatoid arthritis,
		transcription through the	systemic lupus erythematosis,
		NFKB response element that	multiple sclerosis and/or as
		may be used or rountinely	described below) and
		modified to test NFKB-	immunodeficiencies (e.g., as
		response element activity of	described below). Preferred
		polypeptides of the invention	indications also include
		(including antibodies and	neoplastic diseases (e.g.,
		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Berger et al., Gene	below under
		66:1-10 (1998); Cullen and	"Hyperproliferative
		Malm, Methods in Enzymol	Disorders"). Preferred
		216:362-368 (1992); Henthorn	indications include neoplasms
		et al., Proc Natl Acad Sci USA	and cancer, such as, for
		85:6342-6346 (1988); Marone	example, leukemia, lymphoma,
		et al, Int Arch Allergy	melanoma, and prostate,
		Immunol 114(3):207-17	breast, lung, colon, pancreatic,
		(1997), the contents of each of	esophageal, stomach, brain,
		which are herein incorporated	liver, urinary tract cancers and
		by reference in its entirety.	as described below under
		Basophils that may be used	"Hyperproliferative
		according to these assays are	Disorders".
•		publicly available (e.g.,	
		through the ATCC).	
		Exemplary human basophil	

	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkin's lymphoma, non-Hodgkin's symphoma, non-Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	
cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity	of polypeptides of the invention (including antibodies
	Activation of transcription through GAS response element in immune cells (such as T-cells).	,
	HNHOD46 749	
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Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies	(e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated	immune response. Additional preferred indications include inflammation and inflammatory disorders.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with	chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is
and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol	155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety.	Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly	ATCC).	
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	•		Preferred indications include anemia, pancytopenia,
	·		anemia, pancytopenia,
·	·		, ,
	·		leukopenia, thrombocytopenia,
	•		acute lymphocytic anemia
			(ALL), plasmacytomas,
			multiple myeloma, arthritis,
			AIDS, granulomatous disease,
			inflammatory bowel disease,
			sepsis, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues,
			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,
			meningitis, Lyme Disease, and
			asthma and allergy.
HNHOD46 749	Activation of	Assays for the activation of	Highly preferred indications
	transcription	transcription through the	include inflammation and
	through NFKB	NFKB response element are	inflammatory disorders.
	response element in	well-known in the art and may	Highly preferred indications
	immune cells (such	be used or routinely modified	include blood disorders (e.g.,
	as T-cells).	to assess the ability of	as described below under
	-	polypeptides of the invention	"Immune Activity", "Blood-
		(including antibodies and	Related Disorders", and/or
		agonists or antagonists of the	"Cardiovascular Disorders").
		invention) to regulate NFKB	Highly preferred indications
		transcription factors and	include autoimmune diseases
		modulate expression of	(e.g., rheumatoid arthritis,
		immunomodulatory genes.	systemic lupus erythematosis,

multiple sclerosis and/or as described below), and	immunodeficiencies (e.g., as	described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also
Exemplary assays for transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the MOLT4, that may	be used according to these	assays are publicly available	(e.g., through the ATCC).				
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include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
	749
	HNHOD46

Exemplary assays for Highly preferred indications
Exemplary assays for
Exemplary assays for transcription through the SRF
transcription through the SRE

	malignant glioma), solid	solid
	tumors, and prostate, breast,	, breast,
	lung, colon, pancreatic,	tic,
	esophageal, stomach, brain,	ı, brain,
	liver and urinary cancer. Other	icer. Other
	preferred indications include	include
	benign dysproliferative	ive
	disorders and pre-neoplastic	oplastic
	conditions, such as, for	for
	example, hyperplasia,	a,
	metaplasia, and/or dysplasia.	ysplasia.
	Preferred indications include	sinclude
	anemia, pancytopenia,	ia,
	leukopenia, thrombocytopenia,	cytopenia,
	Hodgkin's disease, acute	icute
	lymphocytic anemia (ALL),	(ALL),
	plasmacytomas, multiple	tiple
	myeloma, Burkitt's lymphoma,	lymphoma,
	arthritis, AIDS, granulomatous	ulomatous
	disease, inflammatory bowel	ry bowel
	disease, neutropenia,	
	neutrophilia, psoriasis,	is,
	suppression of immune	ne
	reactions to transplanted	nted
	organs and tissues, hemophilia,	emophilia,
	hypercoagulation, diabetes	abetes
	mellitus, endocarditis,	S,
-	meningitis, Lyme Disease,	isease,
	cardiac reperfusion injury, and	njury, and
	asthma and allergy.	An
	additional preferred indication	indication

					is infection (e.g., an infectious disease as described below under "Infectious Disease").
	HNHOD46	749	Activation of transcription	Assays for the activation of transcription through the	Highly preferred indications include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as natural killer	to assess the ability of	as described below under
			cells).	polypeptides of the invention	"Immune Activity", "Blood-
				(Including annoones and agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
-				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
	_			polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative

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Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),			arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	suppression of immune	reactions to transplanted
85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	NK cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to	these assays include the NKL	cell line, which is a human	natural killer cell line	established from the peripheral	blood of a patient with large	granular lymphocytic	leukemia. This IL-2 dependent	suspension culture cell line has	a morphology resembling that	of activated NK cells.						
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					organs, asthma and allergy.
	HNHOD46	749	Activation of	Assays for the activation of	Preferred indications
			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are well-	(e.g., as described below under
			response element in	known in the art and may be	"Hyperproliferative
			immune cells (such	used or routinely modified to	Disorders"), blood disorders
			as T-cells).	assess the ability of	(e.g., as described below under
	_			polypeptides of the invention	"Immune Activity",
				(including antibodies and	"Cardiovascular Disorders",
				agonists or antagonists of the	and/or "Blood-Related
				invention) to modulate growth	Disorders"), and infection
				and other cell functions.	(e.g., an infectious disease as
				Exemplary assays for	described below under
				transcription through the AP1	"Infectious Disease"). Highly
				response element that may be	preferred indications include
				used or routinely modified to	autoimmune diseases (e.g.,
				test AP1-response element	rheumatoid arthritis, systemic
				activity of polypeptides of the	lupus erythematosis, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below) and
				the invention) include assays	immunodeficiencies (e.g., as
				disclosed in Berger et al., Gene	described below). Additional
• • •				66:1-10 (1988); Cullen and	highly preferred indications
				Malm, Methods in Enzymol	include inflammation and
				216:362-368 (1992); Henthorn	inflammatory disorders.
				et al., Proc Natl Acad Sci USA	Highly preferred indications
				85:6342-6346 (1988);	also include neoplastic
				Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
				272(49):30806-30811 (1997);	lymphoma, and/or as described
				Chang et al., Mol Cell Biol	below under
				18(9):4986-4993 (1998); and	"Hyperproliferative

				Fraser et al., Eur J Immunol	Disorders"). Highly preferred
				29(3):838-844 (1999), the	indications include neoplasms
				contents of each of which are	and cancers, such as, leukemia,
				herein incorporated by	lymphoma, prostate, breast,
				reference in its entirety.	lung, colon, pancreatic,
				Human T cells that may be	esophageal, stomach, brain,
				used according to these assays	liver, and urinary cancer. Other
				are publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
				Exemplary human T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the SUPT cell	example, hyperplasia,
				line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
				responsive suspension-culture	Preferred indications include
				cell line.	arthritis, asthma, AIDS,
-					allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
_					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression of
					immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HNHOD46	749	Activation of	Assays for the activation of	A highly preferred
			transcription	transcription through the CD28	embodiment of the invention
			through CD28	response element are well-	includes a method for
			,		

response element in	known in the art and may be	stimulating T cell proliferation.
	used or routinely modified to	An alternative highly preferred
 as T-cells).	assess the ability of	embodiment of the invention
	polypeptides of the invention	includes a method for
	(including antibodies and	inhibiting T cell proliferation.
	agonists or antagonists of the	A highly preferred
	invention) to stimulate IL-2	embodiment of the invention
	expression in T cells.	includes a method for
	Exemplary assays for	activating T cells. An
	transcription through the CD28	alternative highly preferred
	response element that may be	embodiment of the invention
	used or routinely modified to	includes a method for
	test CD28-response element	inhibiting the activation of
	activity of polypeptides of the	and/or inactivating T cells.
	invention (including antibodies	A highly preferred
	and agonists or antagonists of	embodiment of the invention
	the invention) include assays	includes a method for
	disclosed in Berger et al., Gene	stimulating (e.g., increasing)
	66:1-10 (1998); Cullen and	IL-2 production. An alternative
	Malm, Methods in Enzymol	highly preferred embodiment
	216:362-368 (1992); Henthorn	of the invention includes a
	et al., Proc Natl Acad Sci USA	method for inhibiting (e.g.,
	85:6342-6346 (1988);	reducing) IL-2 production.
	McGuire and Iacobelli, J	Additional highly preferred
	Immunol 159(3):1319-1327	indications include
	(1997); Parra et al., J Immunol	inflammation and
	166(4):2437-2443 (2001); and	inflammatory disorders.
	Butscher et al., J Biol Chem	Highly preferred indications
	3(1):552-560 (1998), the	include autoimmune diseases
	contents of each of which are	(e.g., rheumatoid arthritis,
	herein incorporated by	systemic lupus erythematosis,

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multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Highly preferred	indications include neoplastic	diseases (e.g., melanoma, renal	cell carcinoma, leukemia,	lymphoma, and/or as described	below under	.'Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma (e.g.,	metastatic melanoma), renal	cell carcinoma (e.g., metastatic	renal cell carcinoma),	leukemia, lymphoma (e.g., T	cell lymphoma), and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example hyperplacia
reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.		******																		
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A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections	associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is	AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis,	psoriasis, and tropical spasue paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related	Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel

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disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, Hodgkin's lymphoma, non-Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Preferred indications include autoimmine diseases (e. g.,
	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element an are well-known in the art and may be used or routinely D modified to assess the ability in of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate B STAT transcription factors and H modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies en	
		and agon the inver
	Activation of transcription through GAS response element in immune cells (such as T-cells).	
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cell-mediated immune response. Additional highly	inflammation and	inflammatory disorders. An	additional highly preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious	Disease"). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	1 1
cell-resp	pren	infla	addi	indi	infe	belo	Dise	indi	dise	lym]	belo	"Hy	Disc	indi	and	exar	and	oloo	ston	urin	indi	dysl	pre-	as, f	met	Pref	incl	-
transcription through the NFAT response element that	may be used of routiliery modified to test NFAT-	response element activity of	polypeptides of the invention	including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Serfling	et al., Biochim Biophys Acta	1498(1):1-18 (2000); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	
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Ho lyn lyn my artl dis dis sur rea org	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as
may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that
	Activation of transcription through NFKB response element in immune cells (such as T-cells).
	749
	HNHOD46

	may be used or rountinely	described below). An
	modified to test NFKB-	additional highly preferred
	response element activity of	indication is infection (e.g.,
	polypeptides of the invention	AIDS, and/or an infectious
	(including antibodies and	disease as described below
	agonists or antagonists of the	under "Infectious Disease").
	invention) include assays	Highly preferred indications
	disclosed in Berger et al., Gene	include neoplastic diseases
	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
	Malm, Methods in Enzymol	lymphoma, and/or as described
	216:362-368 (1992); Henthorn	below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Gnes 15(2):105-117	indications include neoplasms
	(1997); and Fraser et al.,	and cancers, such
	29(3):838-844 (1999), the	as,melanoma, renal cell
	contents of each of which are	carcinoma, leukemia,
	herein incorporated by	lymphoma, and prostate,
	reference in its entirety. T	breast, lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,
	according to these assays are	liver and urinary cancer. Other
	publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary human T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,
	line, which is a suspension	metaplasia, and/or dysplasia.
	culture of IL-2 and IL-4	Preferred indications also
	responsive T cells.	include anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute

lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis. systemic
	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response
	Activation of transcription through STAT6 response element in immune cells (such as T-cells).
	HNHOD46

element that may be used or	lupus erythematosis, multiple
 routinely modified to test	sclerosis and/or as described
STAT6 response element	below) and
activity of the polypeptides of	immunodeficiencies (e.g., as
the invention (including	described below).
antibodies and agonists or	Preferred indications include
antagonists of the invention)	neoplastic diseases (e.g.,
include assays disclosed in	leukemia, lymphoma,
Berger et al., Gene 66:1-10	melanoma, and/or as described
 (1998); Cullen and Malm,	below under
Methods in Enzymol 216:362-	"Hyperproliferative
368 (1992); Henthorn et al.,	Disorders"). Preferred
Proc Natl Acad Sci USA	indications include neoplasms
 85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
(1998); Moffatt et al.,	prostate, breast, lung, colon,
Transplantation 69(7):1521-	pancreatic, esophageal,
1523 (2000); Curiel et al., Eur	stomach, brain, liver and
J Immunol 27(8):1982-1987	urinary cancer. Other preferred
(1997); and Masuda et al., J	indications include benign
Biol Chem 275(38):29331-	dysproliferative disorders and
29337 (2000), the contents of	pre-neoplastic conditions, such
each of which are herein	as, for example, hyperplasia,
incorporated by reference in its	metaplasia, and/or dysplasia.
entirety. T cells that may be	Preferred indications include
used according to these assays	anemia, pancytopenia,
are publicly available (e.g.,	leukopenia, thrombocytopenia,
through the ATCC).	Hodgkin's disease, acute
Exemplary T cells that may be	lymphocytic anemia (ALL),
used according to these assays	plasmacytomas, multiple
include the SUPT cell line,	myeloma, Burkitt's lymphoma,

			which is a suspension culture of IL-2 and IL-4 responsive T cells.	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious
HNHOG73	750	SEAP in 293/ISRE		Disease").
HNHOG73	750	Activation of	Assays for the activation of	A highly preferred indication
		transcription	transcription through the	is obesity and/or complications
		through cAMP	cAMP response element are	associated with obesity.
		response element	well-known in the art and may	Additional highly preferred
		(CRE) in pre-	be used or routinely modified	indications include weight loss
		adipocytes.	to assess the ability of	or alternatively, weight gain.
			polypeptides of the invention	An additional highly preferred
			(including antibodies and	indication is diabetes mellitus.
			agonists or antagonists of the	An additional highly preferred
			invention) to increase cAMP,	indication is a complication
			regulate CREB transcription	associated with diabetes (e.g.,
			factors, and modulate	diabetic retinopathy, diabetic
			expression of genes involved	nephropathy, kidney disease
			in a wide variety of cell	(e.g., renal failure,
			functions. For example, a	nephropathy and/or other

diseases and disorders as described in the "Renal Disorders" section below),	diabetic neuropathy, nerve disease and nerve damage	(e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the
3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP	signaling pathway. CREB plays a major role in dingenesis and is involved.	aupogenests, and is involved in differentiation into	adipocytes. CRE contains the binding sequence for the	transcription factor CREB	(CRE binding protein).	Exemplary assays for	transcription through the	cAMP response element that	may be used or routinely	modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch	et al., Mol Cell Biol	20(3):1008-1020 (2000); and	Klemm et al., J Biol Chem	273:917-923 (1998), the
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			contents of each of which are herein incorporated by reference in its entirety. Preadipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays	"Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). Additional highly preferred indications are complications associated with insulin resistance.
HNHOG73	750	Activation of transcription through NFKB response element in immune cells (such as basophils).	conditions known in the art. This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders.

-	tion		agonists or antagonists of the as described below under	invention) to regulate NFKB "Immune Activity", and			immunomodulatory genes. include autoimmune diseases	Exemplary assays for (e.g., rheumatoid arthritis,	transcription through the systemic lupus erythematosis,	NFKB response element that multiple sclerosis and/or as	may be used or rountinely described below) and	modified to test NFKB- immunodeficiencies (e.g., as	response element activity of described below). Preferred	polypeptides of the invention indications also include	(including antibodies and neoplastic diseases (e.g.,	agonists or antagonists of the leukemia, lymphoma,		ene	66:1-10 (1998); Cullen and "Hyperproliferative	_	216:362-368 (1992); Henthorn indications include neoplasms	et al., Proc Natl Acad Sci USA and cancer, such as, for	85:6342-6346 (1988); Marone example, leukemia, lymphoma,	et al, Int Arch Allergy melanoma, and prostate,	Immunol 114(3):207-17 breast, lung, colon, pancreatic,	(1997), the contents of each of esophageal, stomach, brain,	which are herein incorporated liver, urinary tract cancers and	by reference in its entirety.	Basophils that may be used "Hyperproliferative	according to these assays are Disorders".	publicly available (e.g.,
	polypepti	(including	agonists o	invention	transcript	modulate	nonumui	Exemplar	transcript	NFKB rea	may be us	modified	response	polypepti	(including	agonists o	invention	disclosed	66:1-10 (Malm, M	216:362-3	et al., Pro	85:6342-6	et al, Int	lonumul Immunol	(1997), th	which are	by referen	Basophils	according	publicly a
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			through the ATCC). Exemplary human basophil	
			cell lines that may be used	
			according to these assays	
			include Ku812, originally	
			established from a patient with	
			chronic myelogenous	
			leukemia. It is an immature	
			prebasophilic cell line that can	
			be induced to differentiate into	
91			mature basophils.	
HNHOG73	750	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as natural killer	routinely modified to assess	highly preferred embodiment
		cells).	the ability of polypeptides of	of the invention includes a
			the invention (including	method for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth and upregulate the	Activity", "Blood-Related
			function of growth-related	Disorders", and/or
			genes in many cell types.	"Cardiovascular Disorders"),
			Exemplary assays for	Highly preferred indications
			transcription through the SRE	include autoimmune diseases
			that may be used or routinely	(e.g., rheumatoid arthritis,
			modified to test SRE activity	systemic lupus erythematosis,

Crohn"s disease, multiple sclerosis and/or as described	below), immunodeficiencies (e.g., as described below),		immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other
of the polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.					
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751 IL-13 in HMC				preferred	preferred indications include
751 IL-13 in HMC				benign d	benign dysproliferative
751 IL-13 in HMC				disorders	disorders and pre-neoplastic
751 IL-13 in HMC				condition	conditions, such as, for
751 IL-13 in HMC				example	example, hyperplasia,
751 IL-13 in HMC				metaplas	metaplasia, and/or dysplasia.
751 IL-13 in HMC				Preferred	Preferred indications include
751 IL-13 in HMC				anemia, l	anemia, pancytopenia,
751 IL-13 in HMC				leukoper	leukopenia, thrombocytopenia,
751 IL-13 in HMC				Hodgkin	Hodgkin's disease, acute
751 IL-13 in HMC		,		lymphoc	lymphocytic anemia (ALL),
751 IL-13 in HMC				plasmac	plasmacytomas, multiple
751 IL-13 in HMC				myelom	myeloma, Burkitt's lymphoma,
751 IL-13 in HMC				arthritis,	arthritis, AIDS, granulomatous
751 IL-13 in HMC				disease,	disease, inflammatory bowel
751 IL-13 in HMC				disease,	disease, neutropenia,
751 IL-13 in HMC				neutroph	neutrophilia, psoriasis,
751 IL-13 in HMC				suppress	suppression of immune
751 IL-13 in HMC				reactions	reactions to transplanted
751 IL-13 in HMC				organs a	organs and tissues, hemophilia,
751 IL-13 in HMC				hypercos	hypercoagulation, diabetes
751 IL-13 in HMC				mellitus,	mellitus, endocarditis,
751 IL-13 in HMC				meningi	meningitis, Lyme Disease,
751 IL-13 in HMC				cardiac r	cardiac reperfusion injury, and
751 IL-13 in HMC				asthma a	asthma and allergy. An
751 IL-13 in HMC				addition	additional preferred indication
751 IL-13 in HMC				is infecti	is infection (e.g., an infectious
751 IL-13 in HMC				disease a	disease as described below
751				under "I	under "Infectious Disease").
751	TB126	751	IL-13 in HMC		
/31	HNTB126	751	IL-10 in Human T-		

		cell 2B9		
HNTBI26	751	Production of IL-8	Assays measuring production	Highly preferred indications
		by by endothelial	of IL-8 are well known in the	include immunological and
		cells (such as	art and may be used or	inflammatory disorders (e.g.,
		Human Umbilical	routinely modified to assess	such as allergy, asthma,
		Cord Endothelial	the ability of polypeptides of	leukemia, etc. and as described
		Cells).	the invention (including	below under "Immune
			antibodies and agonists or	Activity", and "Blood-Related
			antagonists of the invention) to	Disorders"). Highly preferred
			regulate production and/or	indications also includie
			secretion of IL-8. For	autoimmune disorders (e.g.,
			example, FMAT may be used	rheumatoid arthritis, systemic
			or routinely modified to assess	lupus erythematosis, Crohn"s
			the ability of polypeptides of	disease, multiple sclerosis
			the invention (including	and/or as described below),
			antibodies and agonists or	neoplastic disorders (e.g.,
			antagonists of the invention) to	organ cancers such as lung,
			regulate production and/or	liver, colon cancer, and/or as
			secretion of IL-8 from	described below under
			endothelial cells (such as	"Hyperproliferative
			human umbilical vein	Disorders"), and
			endothelial cells (HUVEC)).	cardiovascular disorders (e.g.
			HUVECs are endothelial cells	such as described below under
			which line venous blood	"Cardiovascular Disorders").
			vessels, and are involved in	Preferred indications include
			functions that include, but are	thrombosis, bacteremia and
			not limited to, angiogenesis,	sepsis syndrome and
			vascular permeability, vascular	consequent complications
			tone, and immune cell	(such as acute respiratory
			extravasation. Endothelial	distress syndrome and
			cells play a pivotal role in the	systemic ischemia-reperfusion

HNTBI26 HNTBI26	751	IL-8 in Normal Human Bronchial Epitheliae Regulation of apoptosis in pancreatic beta	inflammation and secretion of IL-8 may play an important role in recruitment and activation of immune cells such as neutrophils, macrophages, and lymphocytes. Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be	restnosis and atherosclerosis. A highly preferred indication is diabetes mellitus. An additional highly preferred
		cells.	used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and progression of diabetes. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental

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confusion, drowsiness,	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).		indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,
invention) include the assays disclosed in Loweth AC et	al., FEBS Lett, 400(3):285-8	(1997); Saini, KS, et al.,	Biochem Mol Biol Int,	39(6):1229-36 (1996);	Krautheim, A., et al., Br J	Pharmacol, 129(4):687-94	(2000); Chandra J, et al.,	Diabetes, 50 Suppl 1:S44-7	(2001); Suk K, et al., J	Immunol, 166(7):4481-9	(2001); Tejedo J, et al., FEBS	Lett, 459(2):238-43 (1999);	Zhang, S., et al., FEBS Lett,	455(3):315-20 (1999); Lee et	al., FEBS Lett 485(2-3): 122-	126 (2000); Nor et al., J Vasc	Res 37(3): 209-218 (2000);	and Karsan and Harlan, J	Atheroscler Thromb 3(2): 75-	80 (1996); the contents of each	of which are herein	incorporated by reference in its	entirety. Pancreatic cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC)	and/or may be routinely	generated. Exemplary	pancreatic cells that may be
		_																								~			

			used according to these assays include RIN-m. RIN-m is a rat adherent pancreatic beta cell insulinoma cell line derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al.	weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
HNTBI26	751	Caspase (+paclitaxel) in SW480		
HNTBL27	752	Regulation of apoptosis in pancreatic beta cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and progression of diabetes.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve

and one can be compared to the compared on	(c a distance distance)
apopiosis iliai iliay de useu oi	(e.g., due to diabelic
routinely modified to test	neuropathy), blood vessel
capase apoptosis activity of	blockage, heart disease, stroke,
polypeptides of the invention	impotence (e.g., due to diabetic
(including antibodies and	neuropathy or blood vessel
agonists or antagonists of the	blockage), seizures, mental
invention) include the assays	confusion, drowsiness,
disclosed in: Loweth, AC, et	nonketotic hyperglycemic-
al., FEBS Lett, 400(3):285-8	hyperosmolar coma,
(1997); Saini, KS, et al.,	cardiovascular disease (e.g.,
Biochem Mol Biol Int,	heart disease, atherosclerosis,
39(6):1229-36 (1996);	microvascular disease,
Krautheim, A., et al., Br J	hypertension, stroke, and other
Pharmacol, 129(4):687-94	diseases and disorders as
(2000); Chandra J, et al.,	described in the
Diabetes, 50 Suppl 1:S44-7	"Cardiovascular Disorders"
(2001); Suk K, et al., J	section below), dyslipidemia,
Immunol, 166(7):4481-9	endocrine disorders (as
(2001); Tejedo J, et al., FEBS	described in the "Endocrine
Lett, 459(2):238-43 (1999);	Disorders" section below),
Zhang, S., et al., FEBS Lett,	neuropathy, vision impairment
(455(3):315-20 (1999); Lee et	(e.g., diabetic retinopathy and
al., FEBS Lett 485(2-3): 122-	blindness), ulcers and impaired
126 (2000); Nor et al., J Vasc	wound healing, and infection
Res 37(3): 209-218 (2000);	(e.g., infectious diseases and
and Karsan and Harlan, J	disorders as described in the
Atheroscler Thromb 3(2): 75-	"Infectious Diseases" section
80 (1996); the contents of each	below, especially of the
of which are herein	urinary tract and skin), carpal
incorporated by reference in its	
· · · · · · · · · · · · · · · · · · ·	capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Loweth, AC, et al., FEBS Lett, 400(3):285-8 (1997); Saini, KS, et al., Biochem Mol Biol Int, 39(6):1229-36 (1996); Krautheim, A., et al., Br J Pharmacol, 129(4):687-94 (2000); Chandra J, et al., Diabetes, 50 Suppl 1:S44-7 (2001); Suk K, et al., J Immunol, 166(7):4481-9 (2001); Suk K, et al., J Immunol, 166(7):4481-9 (2001); Suk K, et al., J A485(3):315-20 (1999); Lee et al., FEBS Lett, 455(3):315-20 (1999); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein irts

derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polynentide	insulin resistance.
Production of IL-10 and activation of T-cells.	

rheumatoid arthritis, systemic	lupus erythematosis, Crohn"s	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response.																					
inhibit production of IL-10	and/or activation of T-cells.	Exemplary assays that may be	used or routinely modified to	assess the ability of	polypeptides and antibodies of	the invention (including	agonists or antagonists of the	invention) to modulate IL-10	production and/or T-cell	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be	used according to these assays	include Th2 cells. IL10	secreted from Th2 cells may be	measured as a marker of Th2	cell activation. Th2 cells are	a class of T cells that secrete
			-														•					-			-			-		

	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,
IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for
	Production of TNF alpha by dendritic cells
	753
	HNTCE26

systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below),	boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and	inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications	include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and	lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other
immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition	of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention	(including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999): Rowland et al.,	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J	(1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety.

			be used according to these assays may be isolated using	preferred indications include benign dysproliferative
		-	techniques disclosed herein or	disorders and pre-neoplastic
			otherwise known in the art.	conditions, such as, for
			Human dendritic cells are	example, hyperplasia,
			antigen presenting cells in	metaplasia, and/or dysplasia.
			suspension culture, which,	Preferred indications include
			when activated by antigen	anemia, pancytopenia,
			and/or cytokines, initiate and	leukopenia, thrombocytopenia,
			upregulate T cell proliferation	Hodgkin's disease, acute
			and functional activities.	lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
		-		arthritis, AIDS, granulomatous
		-		disease, inflammatory bowel
				disease, neutropenia,
			-	neutrophilia, psoriasis,
			-	suppression of immune
		-		reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
			-	diabetes mellitus, endocarditis,
			-	meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HNTCE26	753	CD69 in Human T cells		

HNTCE26	753	Stimulation of	Assays for measuring secretion	A highly preferred
		insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
_		from pancreatic	the art and may be used or	An additional highly preferred
		beta cells.	routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease
			antagonists of the invention) to	(e.g., renal failure,
			stimulate insulin secretion.	nephropathy and/or other
			For example, insulin secretion	diseases and disorders as
			is measured by FMAT using	described in the "Renal
			anti-rat insulin antibodies.	Disorders" section below),
			Insulin secretion from	diabetic neuropathy, nerve
			pancreatic beta cells is	disease and nerve damage
			upregulated by glucose and	(e.g., due to diabetic
			also by certain	neuropathy), blood vessel
			proteins/peptides, and	blockage, heart disease, stroke,
			disregulation is a key	impotence (e.g., due to diabetic
			component in diabetes.	neuropathy or blood vessel
			Exemplary assays that may be	blockage), seizures, mental
	***		used or routinely modified to	confusion, drowsiness,
			test for stimulation of insulin	nonketotic hyperglycemic-
			secretion (from pancreatic	hyperosmolar coma,
			cells) by polypeptides of the	cardiovascular disease (e.g.,
			invention (including antibodies	heart disease, atherosclerosis,
_			and agonists or antagonists of	microvascular disease,
			the invention) include assays	hypertension, stroke, and other
			disclosed in: Ahren, B., et al.,	diseases and disorders as
			Am J Physiol, 277(4 Pt	described in the
			2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
			al., Endocrinology,	section below), dyslipidemia,

			138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett,	endocrine disorders (as described in the "Endocrine
			377(2):237-9 (1995); and,	Disorders" section below),
			Miraglia S et. al., Journal of	neuropathy, vision impairment
			Biomolecular Screening,	(e.g., diabetic retinopathy and
			4:193-204 (1999), the contents	blindness), ulcers and impaired
			of each of which is herein	wound healing, and infection
			incorporated by reference in its	(e.g., infectious diseases and
			entirety. Pancreatic cells that	disorders as described in the
			may be used according to these	"Infectious Diseases" section
			assays are publicly available	below, especially of the
			(e.g., through the ATCC)	urinary tract and skin), carpal
			and/or may be routinely	tunnel syndrome and
			generated. Exemplary	Dupuytren's contracture).
			pancreatic cells that may be	An additional highly preferred
			used according to these assays	indication is obesity and/or
			include rat INS-1 cells. INS-1	complications associated with
			cells are a semi-adherent cell	obesity. Additional highly
			line established from cells	preferred indications include
			isolated from an X-ray induced	weight loss or alternatively,
			rat transplantable insulinoma.	weight gain. Aditional
			These cells retain	highly preferred indications are
			characteristics typical of native	complications associated with
			pancreatic beta cells including	insulin resistance.
			glucose inducible insulin	
			secretion. References: Asfari	
			et al. Endocrinology 1992	
			130:167.	
HNTCE26	753	Production of	Assays for measuring	Preferred embodiments of the
		ICAM-1	expression of ICAM-1 are	invention include using
			well-known in the art and may	polypeptides of the invention

	:	adipocytes	to assess the ability of	diabetes (e.g., diabetic
•		•	polypeptides of the invention	retinopathy, diabetic
			(including antibodies and	nephropathy, kidney disease
			agonists or antagonists of the	(e.g., renal failure,
			invention) to activate the	nephropathy and/or other
			DMEF1 response element in a	diseases and disorders as
			reporter construct (such as that	described in the "Renal
			containing the GLUT4	Disorders" section below),
			promoter) and to regulate	diabetic neuropathy, nerve
			insulin production. The	disease and nerve damage
			DMEF1 response element is	(e.g., due to diabetic
		-	present in the GLUT4	neuropathy), blood vessel
			promoter and binds to MEF2	blockage, heart disease, stroke,
			transcription factor and another	impotence (e.g., due to diabetic
			transcription factor that is	neuropathy or blood vessel
	-		required for insulin regulation	blockage), seizures, mental
			of Glut4 expression in skeletal	confusion, drowsiness,
-			muscle. GLUT4 is the primary	nonketotic hyperglycemic-
			insulin-responsive glucose	hyperosmolar coma,
			transporter in fat and muscle	cardiovascular disease (e.g.,
			tissue. Exemplary assays that	heart disease, atherosclerosis,
		- 44	may be used or routinely	microvascular disease,
	- 11		modified to test for DMEF1	hypertension, stroke, and other
			response element activity (in	diseases and disorders as
			adipocytes and pre-adipocytes)	described in the
_	-		by polypeptides of the	"Cardiovascular Disorders"
			invention (including antibodies	section below), dyslipidemia,
			and agonists or antagonists of	endocrine disorders (as
			the invention) include assays	described in the "Endocrine
			disclosed in Thai, M.V., et al., J	Disorders" section below),
			Biol Chem, 273(23):14285-92	neuropathy, vision impairment

		(1998): Mora. S., et al., J Biol	(e.g., diabetic retinopathy and
 	5	Chem, 275(21):16323-8	blindness), ulcers and impaired
	(2)	(2000); Liu, M.L., et al., J Biol	wound healing, and infection
	<u>, む</u>	Chem, 269(45):28514-21	(e.g., infectious diseases and
	(1)	(1994); "Identification of a 30-	disorders as described in the
	eq _	base pair regulatory element	"Infectious Diseases" section
	an	and novel DNA binding	below, especially of the
		protein that regulates the	urinary tract and skin). An
	n <mark>i</mark>	human GLUT4 promoter in	additional highly preferred
	tre	transgenic mice", J Biol Chem.	indication is obesity and/or
	20	2000 Aug 4;275(31):23666-73;	complications associated with
	Be	Berger, et al., Gene 66:1-10	obesity. Additional highly
	(1)	(1988); and, Cullen, B., et al.,	preferred indications include
	M	Methods in Enzymol.	weight loss or alternatively,
	21	216:362–368 (1992), the	weight gain. Additional highly
	00	contents of each of which is	preferred indications are
	he	herein incorporated by	complications associated with
	- re	reference in its entirety.	insulin resistance.
	A	Adipocytes and pre-adipocytes	
	th th	that may be used according to	
	th th	these assays are publicly	
	av	available (e.g., through the	
	A	ATCC) and/or may be	
	ro	routinely generated.	
	<u> </u>	Exemplary cells that may be	
	sn	used according to these assays	
	u. h	include the mouse 3T3-L1 cell	
	ıil	line which is an adherent	
	ш	mouse preadipocyte cell line.	
	<u> </u>	Mouse 3T3-L1 cells are a	
	00	continuous substrain of 3T3	

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	A highly preferred indication is obesity and/or complications	associated with obesity.	Additional highly preferred	indications include weight loss	or alternatively, weight gain.	indication is diabetes mellitus.	An additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel
fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	Assays for the activation of	cAMP response element are	well-known in the art and may	be used or routinely modified	to assess the ability of	fincluding antibodies and	agonists or antagonists of the	invention) to increase cAMP,	regulate CREB transcription	factors, and modulate	expression of genes involved	in a wide variety of cell	functions. For example, a	3T3-L1/CRE reporter assay	may be used to identify factors	that activate the cAMP	signaling pathway. CREB	plays a major role in	adipogenesis, and is involved	in differentiation into	adipocytes. CRE contains the	binding sequence for the	transcription factor CREB
	Activation of	through cAMP	response element	(CRE) in pre-	adipocytes.																		
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	(CRE hinding protein)	blockage) seizures mental
	Towns process.	confinctor dromoings
	Exemplary assays for	confusion, drowsiness,
	transcription through the	nonketotic hyperglycemic-
	cAMP response element that	hyperosmolar coma,
	may be used or routinely	cardiovascular disease (e.g.,
	modified to test cAMP-	heart disease, atherosclerosis,
	response element activity of	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in Berger et al., Gene	section below), dyslipidemia,
	66:1-10 (1998); Cullen and	endocrine disorders (as
	Malm, Methods in Enzymol	described in the "Endocrine
	216:362-368 (1992); Henthorn	Disorders" section below),
	et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
	85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
	et al., Mol Cell Biol	blindness), ulcers and impaired
	20(3):1008-1020 (2000); and	wound healing, and infection
****	Klemm et al., J Biol Chem	(e.g., infectious diseases and
	273:917-923 (1998), the	disorders as described in the
	contents of each of which are	"Infectious Diseases" section
	herein incorporated by	below, especially of the
	reference in its entirety. Pre-	urinary tract and skin), carpal
	adipocytes that may be used	tunnel syndrome and
	according to these assays are	Dupuytren's contracture).
	publicly available (e.g.,	Additional highly preferred
	through the ATCC) and/or	indications are complications
	may be routinely generated.	associated with insulin
	Exemplary mouse adipocyte	resistance.
	cells that may be used	

	s d d s
	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve diabetic neuropathy, nerve disease and nerve damage
according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or
·	Activation of transcription through serum response element in pre-adipocytes.
	754
	HNTNI01

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(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below). Additional highly	preferred indications are	complications associated with	insulin resistance.
antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.
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CITO		s,			led pa	nne	lers	under	-	.s.,),	.;	emic	lhn"s	.s	w),	., as	ng an	nune	ly,	. <u>.</u>	ıse.									
red indicat	ia, allergy,	ity reaction	, and	disorders.	ghly prefer	clude imm	ietic disor	ibed below	ivity", and	ed Disorde	diseases (e.	thritis, sys	natosis, Cro	iple scleros	cribed belo	iencies (e.g	ow), boosti	ediated im	alternative	n eosinoph	nune respo									
Highly preferred indications	include asthma, allergy,	hypersensitivity reactions,	inflammation, and	inflammatory disorders.	Additional highly preferred	indications include immune	and hematopoietic disorders	(e.g., as described below under	"Immune Activity", and	"Blood-Related Disorders"),	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, Crohn"s	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below), boosting an	eosinophil-mediated immune	response and, alternatively,	suppressing an eosinophil-	mediated immune response.									
																						gonists of	le assays	et al., Gene	len and	Inzymol	; Henthorn	d Sci USA		pool
Assays for the activation of	transcription through the	Gamma Interferon Activation	Site (GAS) response element	are well-known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	gene expression (commonly	via STAT transcription factors)	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood
Assays	transcri	Gamm	Site (G	are wel	may be	modifie	of poly	inventi	and ago	the inv	gene ex	via ST	involve	cell fur	assays	through	elemen	routine	GAS-re	of poly	inventi	and ago	the inv	disclos	66:1-10	Malm,	216:36	et al., F	85:634	Matika
Activation of	transcription	through GAS	response element in	immune cells (such	as eosinophils).																									
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HNTNI01																	-													
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93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995); the contents of each of which are	herein incorporated by reference in its entirety. Moreover, exemplary assays that may be used or routinely	modified to assess the ability of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) to activate or inhibit activation of immune	and/or cited in: Mayumi M., "EoL-1, a human eosinophilic	cell line" Leuk Lympnoma; Jun;7(3):243-50 (1992); Bhattacharya S, "Granulocyte	macrophage colony- stimulating factor and interleukin-5 activate STAT5	and induce CIS1 mRNA in human peripheral blood	Mol Biol; Mar;24(3):312-6	"Engagement of the CrkL adapter in interleukin-5	signaling in eosinophils" J Biol
		·								

	Highly preferred indications include asthma, allergy, hypersensitivity reactions, and inflammation. Preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), immunological disorders, inflammation and
Chem; Oct 20;275(42):33167-75 (2000); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are a type of immune cell important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB
·	Activation of transcription through NFKB response element in immune cells (such as EOL1 cells).
(754
	HNTNI01

			EOL-1 cells) may link the NFKB element to a repeorter gene and binds to the NFKB transcription factor, which is upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important in the allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Eol-1 is a human	
HNTNI01	754	Regulation of transcription of Malic Enzyme in adipocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesisn is	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve

	stimulted by insulin. ME	disease and nerve damage
	promoter contains two direct	(e.g., due to diabetic
	repeat (DR1)- like elements	neuropathy), blood vessel
	MEp and MEd identified as	blockage, heart disease, stroke,
	putative PPAR response	impotence (e.g., due to diabetic
	elements. ME promoter may	neuropathy or blood vessel
	also responds to AP1 and other	blockage), seizures, mental
	transcription factors.	confusion, drowsiness,
	Exemplary assays that may be	nonketotic hyperglycemic-
	used or routinely modified to	hyperosmolar coma,
	test for regulation of	cardiovascular disease (e.g.,
	transcription of Malic Enzyme	heart disease, atherosclerosis,
	(in adipoocytes) by	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
-	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in: Streeper, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	Disorders" section below),
	Endocrinol, 8(10):1361-9	neuropathy, vision impairment
	(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
	Biol Chem, 274(25):17997-	blindness), ulcers and impaired
	8004 (1999); Ijpenberg, A., et	wound healing, and infection
	al., J Biol Chem,	(e.g., infectious diseases and
	272(32):20108-20117 (1997);	disorders as described in the
	Berger, et al., Gene 66:1-10	"Infectious Diseases" section
	(1988); and, Cullen, B., et al.,	below, especially of the
	Methods in Enzymol.	urinary tract and skin), carpal
	216:362–368 (1992), the	tunnel syndrome and

			contents of each of which is herein incorporated by	Dupuytren's contracture). An additional highly preferred
			reference in its entirety. Hepatocytes that may be used	indication is obesity and/or complications associated with
			according to these assays are	obesity. Additional highly
			publicly available (e.g.,	preferred indications include
			through the ATCC) and/or	weight loss or alternatively,
			may be routinely generated.	weight gain. Aditional
			Exemplary hepatocytes that	highly preferred indications are
			may be used according to these	complications associated with
			assays includes the H4IIE rat	insulin resistance.
			liver hepatoma cell line.	
HNTNI01	754	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the GATA-3	include allergy, asthma, and
		through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and
			activation of transcription	inflammatory disorders.
		-	through the GATA3 response	Preferred indications also
			element are well-known in the	include blood disorders (e.g.,
			art and may be used or	as described below under
			routinely modified to assess	"Immune Activity", "Blood-
			the ability of polypeptides of	Related Disorders", and/or
			the invention (including	"Cardiovascular Disorders").
			antibodies and agonists or	Preferred indications include
			antagonists of the invention) to	autoimmune diseases (e.g.,
			regulate GATA3 transcription	rheumatoid arthritis, systemic
			factors and modulate	lupus erythematosis, multiple

	λd	expression of mast cell genes	sclerosis and/or as described
	S . E	important for immiline response	helow) and
 -		Ipottant tot minimus response	borow) and
	de	development. Exemplary	immunodeliciencies (e.g., as
	ass	assays for transcription	described below). Preferred
	thr	through the GATA3 response	indications include neoplastic
	ele	element that may be used or	diseases (e.g., leukemia,
		routinely modified to test	lymphoma, melanoma,
	<u>'5</u>	GATA3-response element	prostate, breast, lung, colon,
	aci	activity of polypeptides of the	pancreatic, esophageal,
	ni	invention (including antibodies	stomach, brain, liver, and
	an	and agonists or antagonists of	urinary tract cancers and/or as
	the	the invention) include assays	described below under
	dis	disclosed in Berger et al., Gene	"Hyperproliferative
	99	66:1-10 (1998); Cullen and	Disorders"). Other preferred
	W	Malm, Methods in Enzymol	indications include benign
	21	216:362-368 (1992); Henthorn	dysproliferative disorders and
	et	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
	85	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	et	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
	Ō	Quant Biol 64:563-571 (1999);	Preferred indications include
 -	RC	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
	I f	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	1)	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
	<u> </u>	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
	H	Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
	14	14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
	00	contents of each of which are	lymphoma, arthritis, AIDS,
	he	herein incorporated by	granulomatous disease,
	re	reference in its entirety. Mast	inflammatory bowel disease,
	<u> </u>	cells that may be used	sepsis, neutropenia,
	ac	according to these assays are	neutrophilia, psoriasis,

			publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to	suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoamlation diabetes
	*		these assays include the HMC-	mellitus, endocarditis,
			l cell line, which is an	meningitis, and Lyme Disease.
			immature human mast cell line	
			established from the peripheral	
			olood of a patient with mast cell leukemia, and exhibits	
	-		many characteristics of	
			immature mast cells.	
HNTNI01	754	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the NFAT	include allergy, asthma, and
		through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
-		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
	<u></u>		production. Assays for the	inflammation and
			activation of transcription	inflammatory disorders.
			through the Nuclear Factor of	Preferred indications also
			Activated T cells (NFAT)	include blood disorders (e.g.,
			response element are well-	as described below under
			known in the art and may be	"Immune Activity", "Blood-
			used or routinely modified to	Related Disorders", and/or
			assess the ability of	"Cardiovascular Disorders").
			polypeptides of the invention	Preferred indications include
			(including antibodies and	autoimmune diseases (e.g.,
			agonists or antagonists of the	rheumatoid arthritis, systemic
			invention) to regulate NFAT	lupus erythematosis, multiple

transcription factors and	sclerosis and/or as described
modulate expression of genes	below) and
involved in	immunodeficiencies (e.g., as
immunomodulatory functions.	described below). Preferred
Exemplary assays for	indications include neoplastic
 transcription through the	diseases (e.g., leukemia,
NFAT response element that	lymphoma, melanoma,
may be used or routinely	prostate, breast, lung, colon,
 modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
(including antibodies and	described below under
 agonists or antagonists of the	"Hyperproliferative
invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
85:6342-6346 (1988); De Boer	Preferred indications include
et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et al., J Immunol	leukemias, Hodgkin's disease,
165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
 al., J Exp Med 188:527-537	granulomatous disease,
(1998), the contents of each of	inflammatory bowel disease,
which are herein incorporated	sepsis, neutropenia,
by reference in its entirety.	neutrophilia, psoriasis,

			Mast cells that may be used according to these assays are	suppression of immune reactions to transplanted
			publicly available (e.g.,	organs and tissues, hemophilia,
			through the ATCC).	hypercoagulation, diabetes
			Exemplary human mast cells	mellitus, endocarditis,
			that may be used according to	meningitis, and Lyme Disease.
			these assays include the HMC-	
			1 cell line, which is an	
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HNTNI01	754	Activation of	This reporter assay measures	Highly preferred indication
		transcription	activation of the NFkB	includes allergy, asthma, and
		through NFKB	signaling pathway in HMC-1	rhinitis. Additional highly
		response element in	human mast cell line.	preferred indications include
		immune cells (such	Activation of NFkB in mast	infection (e.g., an infectious
		as mast cells).	cells has been linked to	disease as described below
			production of certain	under "Infectious Disease"),
			cytokines, such as IL-6 and IL-	and inflammation and
			9. Assays for the activation of	inflammatory disorders.
			transcription through the	Preferred indications include
			NFKB response element are	immunological and
			well-known in the art and may	hempatopoietic disorders (e.g.,
			be used or routinely modified	as described below under
			to assess the ability of	"Immune Activity", and
			polypeptides of the invention	"Blood-Related Disorders").
			(including antibodies and	Preferred indications also
			agonists or antagonists of the	include autoimmune diseases

		invention) to regulate NFKB	(e.g. rheumatoid arthritis.
		transcription factors and	systemic lupus erythematosis.
		modulate expression of	multiple sclerosis and/or as
		immunomodulatory genes.	described below) and
		Exemplary assays for	immunodeficiencies (e.g., as
		transcription through the	described below). Preferred
		NFKB response element that	indications also include
		may be used or rountinely	neoplastic diseases (e.g.,
		modified to test NFKB-	leukemia, lymphoma,
		response element activity of	melanoma, and/or as described
		polypeptides of the invention	below under
		including antibodies and	"Hyperproliferative
		agonists or antagonists of the	Disorders"). Preferred
		invention) include assays	indications include neoplasms
		disclosed in Berger et al., Gene	and cancer, such as, for
		66:1-10 (1998); Cullen and	example, leukemia, lymphoma,
		Malm, Methods in Enzymol	melanoma, and prostate,
		216:362-368 (1992); Henthorn	breast, lung, colon, pancreatic,
		et al., Proc Natl Acad Sci USA	esophageal, stomach, brain,
		85:6342-6346 (1988); Stassen	liver, urinary tract cancers and
		et al, J Immunol 166(7):4391-8	as described below under
		(2001); and Marquardt and	"Hyperproliferative
		Walker, J Allergy Clin	Disorders".
-		Immunol 105(3):500-5 (2000),	
		the contents of each of which	
		are herein incorporated by	
		reference in its entirety. Mast	
		cells that may be used	
	-	according to these assays are	
		publicly available (e.g.,	
		through the ATCC).	

				Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells	
<u>H</u>	HNTNI01	754	Activation of transcription through STAT6 response element in immune cells (such as mast cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element in immune cells (such as in the human HMC-1 mast cell line) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary	Highly preferred indications include allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders. Preferred indications also include hematopoietic and immunological disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), autoimmune diseases (e.g.,
				assays for transcription through the STAT6 response element that may be used or routinely modified to test	rneumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and

activity of the polypeptides of the invention (including antibodies and agonists or antibodies and agonists or include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362- Methods in Methods		
STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Sherman, Immunol Rev 179:48-56 (2001); Malaviya and Uckun, J Immunol 168:421-426 (2002); Masuda et al., J Biol Chem 275(38):29331-29337 (2000); and Masuda et al., J Biol Chem 276:26107-26113 (2001), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-	STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1998); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Sherman, Immunol Rev 179:48-56 (2001); Malaviya and Uckun, J Immunol 168:421-426 (2002); Masuda et al., J Biol Chem 275(38):29331-29337 (2000); and Masuda et al., J Biol Chem 276:26107-26113 (2001), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-	STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Sherman, Immunol Rev 179:48-56 (2001); Malaviya and Uckun, J Immunol 168:421-426 (2002); Masuda et al., J Biol Chem 275(38):2931-29337 (2000); and Masuda et al., J Biol Chem 275(38):2931-29337 (2001); the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-

			immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
HNTNI01	754	Activation of transcription through NFKB response element in immune cells (such as basophils).	This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders. Preferred indications include immunological and hempatopoietic disorders (e.g., as described below under
			invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and	"Immune Activity", and "Blood-Related Disorders"). Preferred indications also include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications also include neoplastic diseases (e.g.,

			agonists or antagonists of the	leukemia. Ivmphoma.
			invention) include assays	melanoma, and/or as described
			disclosed in Berger et al., Gene	below under
			66:1-10 (1998); Cullen and	"Hyperproliferative
			Malm, Methods in Enzymol	Disorders"). Preferred
			216:362-368 (1992); Henthorn	indications include neoplasms
			et al., Proc Natl Acad Sci USA	and cancer, such as, for
			85:6342-6346 (1988); Marone	example, leukemia, lymphoma,
_			et al, Int Arch Allergy	melanoma, and prostate,
			Immunol 114(3):207-17	breast, lung, colon, pancreatic,
			(1997), the contents of each of	esophageal, stomach, brain,
			which are herein incorporated	liver, urinary tract cancers and
			by reference in its entirety.	as described below under
			Basophils that may be used	"Hyperproliferative
			according to these assays are	Disorders".
			publicly available (e.g.,	
			through the ATCC).	
			Exemplary human basophil	
			cell lines that may be used	
 			according to these assays	
			include Ku812, originally	
			established from a patient with	
			chronic myelogenous	
			leukemia. It is an immature	
			prebasophilic cell line that can	
			be induced to differentiate into	
			mature basophils.	
HNTNI01	754	SEAP in		
		Molt4/SRE		
HNTNI01	754	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include blood disorders (e.g.,

	through NFAT	Nuclear Factor of Activated T	as described below under
	response element in	cells (NFAT) response element	"Immune Activity", "Blood-
	immune cells (such	are well-known in the art and	Related Disorders", and/or
	as natural killer	may be used or routinely	"Cardiovascular Disorders").
	cells).	modified to assess the ability	Highly preferred indications
		of polypeptides of the	include autoimmune diseases
		invention (including antibodies	(e.g., rheumatoid arthritis,
		and agonists or antagonists of	systemic lupus erythematosis,
		the invention) to regulate	multiple sclerosis and/or as
-		NFAT transcription factors and	described below),
		modulate expression of genes	immunodeficiencies (e.g., as
		involved in	described below), boosting a T
		immunomodulatory functions.	cell-mediated immune
		Exemplary assays for	response, and suppressing a T
		transcription through the	cell-mediated immune
		NFAT response element that	response. Additional highly
		may be used or routinely	preferred indications include
		modified to test NFAT-	inflammation and
		response element activity of	inflammatory disorders. An
		polypeptides of the invention	additional highly preferred
		(including antibodies and	indication is infection (e.g., an
		agonists or antagonists of the	infectious disease as described
		invention) include assays	below under "Infectious
		disclosed in Berger et al., Gene	Disease"). Preferred
		66:1-10 (1998); Cullen and	indications include neoplastic
		Malm, Methods in Enzymol	diseases (e.g., leukemia,
		216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988);	"Hyperproliferative
		Aramburu et al., J Exp Med	Disorders"). Preferred
		182(3):801-810 (1995); De	indications include neoplasms

			Boer et al., Int J Biochem Cell	and cancers, such as, for
			Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
			Fraser et al., Eur J Immunol	and prostate, breast, lung,
			29(3):838-844 (1999); and	colon, pancreatic, esophageal,
			Yeseen et al., J Biol Chem	stomach, brain, liver and
			268(19):14285-14293 (1993),	urinary cancer. Other preferred
			the contents of each of which	indications include benign
			are herein incorporated by	dysproliferative disorders and
			reference in its entirety. NK	pre-neoplastic conditions, such
			cells that may be used	as, for example, hyperplasia,
			according to these assays are	metaplasia, and/or dysplasia.
			publicly available (e.g.,	Preferred indications also
			through the ATCC).	include anemia, pancytopenia,
			Exemplary human NK cells	leukopenia, thrombocytopenia,
			that may be used according to	Hodgkin's disease, acute
			these assays include the NK-	lymphocytic anemia (ALL),
			YT cell line, which is a human	plasmacytomas, multiple
			natural killer cell line with	myeloma, Burkitt's lymphoma,
			cytolytic and cytotoxic	arthritis, AIDS, granulomatous
			activity.	disease, inflammatory bowel
				disease, sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				asthma and allergy.
HNTNI01	754	SEAP in		
		INDIO/SIAIO		

immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and	inflammatory disorders. Highly preferred indications include blood disorders (e.g.,	as described below under "Immune Activity", "Blood- Related Disorders", and/or "Cardiovascular Disorders"),	and infection (e.g., viral infections, tuberculosis, infections associated with	chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described	below under "Infectious Disease"). An additional preferred indication is	Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia	(ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,
93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by	reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that	may be used according to these assays are publicly available (e.g., through the ATCC).					
			- av				

sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,
	Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the FAS promoter element in a reporter construct and to regulate transcription of FAS, a key enzyme for lipogenesis. FAS promoter is regulated by many transcription factors including SREBP. Insulin increases FAS gene transcription in livers of diabetic mice. This stimulation of transcription is also somewhat glucose
	Regulation of transcription through the FAS promoter element in hepatocytes
	755
	HODDF13

		that may be used or routinely	hyperosmolar coma,
		modified to test for FAS	cardiovascular disease (e.g.,
		promoter element activity (in	heart disease, atherosclerosis,
		hepatocytes) by polypeptides	microvascular disease,
		of the invention (including	hypertension, stroke, and other
		antibodies and agonists or	diseases and disorders as
		antagonists of the invention)	described in the
		include assays disclosed in	"Cardiovascular Disorders"
		Xiong, S., et al., Proc Natl	section below), dyslipidemia,
		Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
		53 (2000); Roder, K., et al.,	described in the "Endocrine
		Eur J Biochem, 260(3):743-51	Disorders" section below),
		(1999); Oskouian B, et al.,	neuropathy, vision impairment
		Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
	-	(1996); Berger, et al., Gene	blindness), ulcers and impaired
		66:1-10 (1988); and, Cullen,	wound healing, and infection
		B., et al., Methods in Enzymol.	(e.g., infectious diseases and
		216:362–368 (1992), the	disorders as described in the
		contents of each of which is	"Infectious Diseases" section
		herein incorporated by	below, especially of the
		reference in its entirety.	urinary tract and skin), carpal
-		Hepatocytes that may be used	tunnel syndrome and
	.,,	according to these assays, such	Dupuytren's contracture).
		as H4IIE cells, are publicly	An additional highly preferred
-		available (e.g., through the	indication is obesity and/or
		ATCC) and/or may be	complications associated with
		routinely generated.	obesity. Additional highly
		Exemplary hepatocytes that	preferred indications include
		may be used according to these	weight loss or alternatively,
		assays include rat liver	weight gain. Aditional
		hepatoma cell line(s) inducible	highly preferred indications are

			with glucocorticoids, insulin, or cAMP derivatives.	complications associated with insulin resistance.
HODDF13	755	Inhibition of	Reporter Assay: construct	
		squalene synthetase	contains regulatory and coding sequence of squalene	
		Evile timiseripuom	synthetase, the first specific	
			enzyme in the cholesterol	
			biosynthetic pathway. See	
			Jiang, et al., J. Biol. Chem.	
			268:12818-128241(993), the	
			contents of which are herein	
			incorporated by reference in its	
			entirety. Cells were treated	
			with SID supernatants, and	
			SEAP activity was measured	
			after 72 hours. HepG2 is a	
			human hepatocellular	
			carcinoma cell line (ATCC	
			HB-8065). See Knowles et al.,	
			Science. 209:497-9 (1980), the	
			contents of which are herein	
			incorporated by reference in its	
			entirety.	
HODDF13	755	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the GATA-3	include allergy, asthma, and
		through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and

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sorders.	ions also	sorders (6	ow under	ty", "Blo	rs", and/c	Disorder	tions incl	eases (e.g	ritis, syst	osis, mul	as descril		icies (e.g.). Prefer	ide neopl	ukemia,	anoma,	lung, col	hageal,	liver, an	cers and	/ under	tive	her prefe	ade benig	disorder	onditions	, hyperpla	or dyspla	tions inc
inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include
inflam	Preferr	include	as desc	nmmI,,	Related	"Cardi	Preferr	autoim	rhenma	lupus e	scleros	below) and	immur	describ	indicat	disease	lymph	prostat	pancre	stomac	urinar	descril	-	Disorc	indical	dysprc	pre-ne	as, for		
l uc	bonse	in the		sess	les of		or	tion) to	ription		genes	esponse	<u> </u>		sponse	ed or	st	ent	of the	tibodies	ists of	ıssays	l., Gene	and	ymol	enthorn	ci USA	Flavell	Symp	(1999);
anscription	TA3 res	ll-knowr	used or	fied to as	olypeptic	including	agonists	the inven	A3 transc	dulate	nast cell	mmune r	Exempla	scription	ATĀ3 res	ay be us	ified to te	nse elem	ypeptides	uding an	r antagor	include a	erger et a); Cullen	ls in Enz	1992); H	tl Acad S	(1988);]	ring Harl	:563-571
activation of transcription	through the GATA3 response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate GATA3 transcription	factors and modulate	expression of mast cell genes	important for immune response	development. Exemplary	assays for transcription	through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);
actival	throug	eleme	art and	routin	the ab	the in	antibo	antago	regula	factor	expre	impor	develo	assays	through	eleme	routin	GAT/	activi	inven	and a	the in	disclo	-1:99	Malm	216:3	et al.,	85:63	et al.,	Quan
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			Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
			J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
			(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
			Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
			Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
			14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
			contents of each of which are	lymphoma, arthritis, AIDS,
			herein incorporated by	granulomatous disease,
			reference in its entirety. Mast	inflammatory bowel disease,
			cells that may be used	sepsis, neutropenia,
			according to these assays are	neutrophilia, psoriasis,
			publicly available (e.g.,	suppression of immune
			through the ATCC).	reactions to transplanted
			Exemplary human mast cells	organs and tissues, hemophilia,
			that may be used according to	hypercoagulation, diabetes
		-	these assays include the HMC-	mellitus, endocarditis,
			1 cell line, which is an	meningitis, and Lyme Disease.
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HODDF13	755	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the NFAT	include allergy, asthma, and
		through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and

Activated relatively and the Nuclear Factor of Activated relatively to Perferred indications also Activated relative for assess the ability of assess the ability of assess the ability of assess the ability of agonists or antagonists of the invention or regulate Network in the art and may be used or routinely modified to test NFAT. Preferred indications include assess the ability of invention or regulate NFAT invention or regulate NFAT invention) to regulate NFAT invention and transcription factors and modulate expression of genes involved in involved in munumomodulatory functions. Exemplary assays for transcription through the NFAT expense element that ymphoma, melahoma, may be used or routinely modified to test NFAT. Presponse lement and may be used or routinely modified to test NFAT. Presponse lement and may be used or routinely protein and malm, Methods in Enzymol 1216:562-5368 (1992); Henthom as, for example, hyperplasia, et al., Proc Nall Acad Sci USA Preferred indications also described below under and involved in many tract cancers and/or as (including antibodies and escribed below). Preferred indications include benign described below under agonists or antagonists of the invention of the preferred indications include benign described below under al., Proc Nall Acad Sci USA Preferred indications also described below under and indications include benign described below under al., Proc Nall Acad Sci USA Preferred indications and/or asplayed and the invention of the preferred indications include benign described below under al., Proc Nall Acad Sci USA Preferred Indications include benign described below under al., Proc Nall Acad Sci USA Preferred indications include benign described below under al., Proc Nall Acad Sci USA Preferred Indications include assays included indications include assays and the invention and the included indications include assays included indications include assays and the invention and the invention and the indications include and the invention and the invention and the in																															
activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well- known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT response element that may be used or routinely modified to test NFAT response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998), Cullen and Malm, Methods in Enzymol 216:36:36:3-388 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:63-42-6346 (1988), De Boer	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	["Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include
	activation of transcription	through the Nuclear Factor of	Activated T cells (NFAT)	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer
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4	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include
et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells
	755
	HODDF13

inflammation and	inflammatory disorders,	immunological disorders,	neoplastic disorders (e.g.	cancer/tumorigenesis), and	cardiovascular disorders (such	as described below under	"Immune Activity", "Blood-	Related Disorders",	"Hyperproliferative Disorders"	and/or "Cardiovascular	Disorders"). Highly preferred	indications include neoplasms	and cancers such as, for	example, leukemia, lymphoma,	melanoma, renal cell	carcinoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.					
(including antibodies and	agonists or antagonists of the	invention) to regulate VCAM	expression. For example,	FMAT may be used to meaure	the upregulation of cell surface	VCAM-1 expresssion in	endothelial cells. Endothelial	cells are cells that line blood	vessels, and are involved in	functions that include, but are	not limited to, angiogenesis,	vascular permeability, vascular	tone, and immune cell	extravasation. Exemplary	endothelial cells that may be	used according to these assays	include human umbilical vein	endothelial cells (HUVEC),	which are available from	commercial sources. The	expression of VCAM	(CD106), a membrane-	associated protein, can be	upregulated by cytokines or	other factors, and contributes	to the extravasation of	lymphocytes, leucocytes and	other immune cells from blood	vessels; thus VCAM	expression plays a role in
(HUVEC))																														
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ınd ıses.			produced A highly preferred
promoting immune and inflammatory responses.		Assays for activation of transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was measured after 48 hours. LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of specific tumoral markers in colon cancer. See, Patan et al., Circ Res, 89(8):732-39 (2001), the contents of which are herein incorporated by reference in its entirety.	IL-6 FMAT. IL-6 is produced by T cells and has strong
	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	Activation of Transcription	Production of IL-6
	755	755	756
	HODDF13	HODDF13	HODDN92

ge l	effects on B cells. IL-6	includes a method for
pd	participates in IL-4 induced	stimulating (e.g., increasing)
60	IgE production and increases	IL-6 production. An alternative
18	IgA production (IgA plays a	highly preferred embodiment
O	role in mucosal immunity).	of the invention includes a
11	IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
Δ̈́	Deregulated expression of IL-6	reducing) IL-6 production. A
ha	has been linked to autoimmune	highly preferrred indication is
ip — — — — — — — — — — — — — — — — — — —	disease, plasmacytomas,	the stimulation or enhancement
iu -	myelomas, and chronic	of mucosal immunity. Highly
hy	hyperproliferative diseases.	preferred indications include
As (As	Assays for immunomodulatory	blood disorders (e.g., as
an	and differentiation factor	described below under
Jd.	proteins produced by a large	"Immune Activity", "Blood-
Va	variety of cells where the	Related Disorders", and/or
xa ex	expression level is strongly	"Cardiovascular Disorders"),
Ice	regulated by cytokines, growth	and infection (e.g., as
fac	factors, and hormones are well	described below under
kn	known in the art and may be	"Infectious Disease"). Highly
sn	used or routinely modified to	preferred indications include
38	assess the ability of	autoimmune diseases (e.g.,
od	polypeptides of the invention	rheumatoid arthritis, systemic
(ir	(including antibodies and	lupus erythematosis, multiple
38	agonists or antagonists of the	sclerosis and/or as described
ii.	invention) to mediate	below) and
ui.	immunomodulation and	immunodeficiencies (e.g., as
di	differentiation and modulate T	described below). Highly
93	cell proliferation and function.	preferred indications also
E	Exemplary assays that test for	include boosting a B cell-
ii.	immunomodulatory proteins	mediated immune response
ev	evaluate the production of	and alternatively suppressing a

			bue 9-11 se dons send	B cell-mediated immune
			the etimulation and	response Highly preferred
				indications indicated
			upregulation of T cell	indications include
			proliferation and functional	inflammation and
			activities. Such assays that	inflammatory
			may be used or routinely	disorders.Additional highly
		•	modified to test	preferred indications include
			immunomodulatory and	asthma and allergy. Highly
			diffferentiation activity of	preferred indications include
-			polypeptides of the invention	neoplastic diseases (e.g.,
			including antibodies and	myeloma, plasmacytoma,
			agonists or antagonists of the	leukemia, lymphoma,
	-		invention) include assays	melanoma, and/or as described
			disclosed in Miraglia et al., J	below under
			Biomolecular Screening 4:193-	"Hyperproliferative
			204(1999); Rowland et al.,	Disorders"). Highly preferred
			"Lymphocytes: a practical	indications include neoplasms
	••		approach" Chapter 6:138-160	and cancers, such as, myeloma,
	-		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
			Immunol 158:2919-2925	lymphoma, melanoma, and
			(1997), the contents of each of	prostate, breast, lung, colon,
			which are herein incorporated	pancreatic, esophageal,
			by reference in its entirety.	stomach, brain, liver and
			Human dendritic cells that may	urinary cancer. Other preferred
			be used according to these	indications include benign
			assays may be isolated using	dysproliferative disorders and
			techniques disclosed herein or	pre-neoplastic conditions, such
			otherwise known in the art.	as, for example, hyperplasia,
			Human dendritic cells are	metaplasia, and/or dysplasia.
			antigen presenting cells in	Preferred indications include
			suspension culture, which,	anemia, pancytopenia,

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leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is
when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies
	Production of MCP-1
	756
	HODDN92
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infection (e.g., an infectious	disease as described below	under "Infectious Disease").	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,
and agonists or antagonists of	life invention) to incurate	immunomodulation, induce	chemotaxis, and modulate	immune cell activation.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of cell	surface markers, such as	monocyte chemoattractant	protein (MCP), and the	activation of monocytes and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); and	Verhasselt et al., J Immunol	158:2919-2925 (1997), the	contents of each of which are
						-	-																	-						
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				herein incorporated by	neutrophilia, psoriasis,
				reference in its entirety.	suppression of immune
_				Human dendritic cells that may	reactions to transplanted
				be used according to these	organs and tissues,
				assays may be isolated using	hemophilia, hypercoagulation,
				techniques disclosed herein or	diabetes mellitus, endocarditis,
				otherwise known in the art.	meningitis (bacterial and
				Human dendritic cells are	viral), Lyme Disease, asthma,
				antigen presenting cells in	and allergy Preferred
				suspension culture, which,	indications also include
				when activated by antigen	neoplastic diseases (e.g.,
				and/or cytokines, initiate and	leukemia, lymphoma, and/or as
				upregulate T cell proliferation	described below under
				and functional activities.	"Hyperproliferative
					Disorders"). Highly preferred
	_				indications include neoplasms
					and cancers, such as, leukemia,
					lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer. Other
					preferred indications include
		-			benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HODDN92	756	Production of	MIP-1alpha FMAT. Assays	A highly preferred
			MIP1alpha	for immunomodulatory	embodiment of the invention
				proteins produced by activated	includes a method for
				dendritic cells that upregulate	stimulating MIP1a production.

An alternative highly preferred embodiment of the invention includes a method for	inhibiting (e.g., reducing) MIP1a production. A highly	preferred indication is infection (e.g., an infectious	disease as described below under "Infectious Disease").	Preferred indications include blood disorders (e.g., as	described below under	"Immune Activity", "Blood- Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,		lymphocytic anemia (ALL),
monocyte/macrophage and T cell chemotaxis are well	used or routinely modified to assess the ability of	polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) to mediate	immunomodulation, modulate chemotaxis, and modulate T	cell differentiation. Exemplary	assays that test for imminomodulatory proteins	evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999). Rowland et al.
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"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Sathhapom and Eremin, J R Coll Surg Edub 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1997); thuman dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and upregulate T cell proliferation and functional activities.	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel	disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted	organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy.		indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925	(1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety.	Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art.	antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	

HODDN92	756	Regulation of	Assays for the regulation of	A highly preferred
		transcription	transcription through the FAS	indication is diabetes mellitus.
		through the FAS	promoter element are well-	An additional highly preferred
		promoter element	known in the art and may be	indication is a complication
		in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
			assess the ability of	diabetic retinopathy, diabetic
			polypeptides of the invention	nephropathy, kidney disease
			including antibodies and	(e.g., renal failure,
			agonists or antagonists of the	nephropathy and/or other
			invention) to activate the FAS	diseases and disorders as
			promoter element in a reporter	described in the "Renal
			construct and to regulate	Disorders" section below),
	-		transcription of FAS, a key	diabetic neuropathy, nerve
			enzyme for lipogenesis. FAS	disease and nerve damage
			promoter is regulated by many	(e.g., due to diabetic
			transcription factors including	neuropathy), blood vessel
			SREBP. Insulin increases FAS	blockage, heart disease, stroke,
			gene transcription in livers of	impotence (e.g., due to diabetic
			diabetic mice. This	neuropathy or blood vessel
			stimulation of transcription is	blockage), seizures, mental
			also somewhat glucose	confusion, drowsiness,
			dependent. Exemplary assays	nonketotic hyperglycemic-
			that may be used or routinely	hyperosmolar coma,
			modified to test for FAS	cardiovascular disease (e.g.,
			promoter element activity (in	heart disease, atherosclerosis,
			hepatocytes) by polypeptides	microvascular disease,
			of the invention (including	hypertension, stroke, and other
			antibodies and agonists or	diseases and disorders as
			antagonists of the invention)	described in the
			include assays disclosed in	"Cardiovascular Disorders"
			Xiong, S., et al., Proc Natl	section below), dyslipidemia,

				Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
				53 (2000); Roder, K., et al.,	described in the "Endocrine
				Eur J Biochem, 260(3):743-51	Disorders" section below),
				(1999); Oskouian B, et al.,	neuropathy, vision impairment
				Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
				(1996); Berger, et al., Gene	blindness), ulcers and impaired
				66:1-10 (1988); and, Cullen,	wound healing, and infection
				B., et al., Methods in Enzymol.	(e.g., infectious diseases and
				216:362–368 (1992), the	disorders as described in the
				contents of each of which is	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety.	urinary tract and skin), carpal
				Hepatocytes that may be used	tunnel syndrome and
				according to these assays, such	Dupuytren's contracture).
-				as H4IIE cells, are publicly	An additional highly preferred
				available (e.g., through the	indication is obesity and/or
				ATCC) and/or may be	complications associated with
				routinely generated.	obesity. Additional highly
-				Exemplary hepatocytes that	preferred indications include
				may be used according to these	weight loss or alternatively,
				assays include rat liver	weight gain. Aditional
				hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
	HODDN92	756	Activation of	This reporter assay measures	Highly preferred indications
			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and

production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists of antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or routinely modified to test GATA3-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al. Proc. Natl. Nacl. Sci. 118A		d sorders. ions also sorders (e.g., ww under y', "Blood-s", and/or Disorders"). ions include ases (e.g., tits, systemic sis, multiple is described is described de neoplastic lkemia, noma, ung, colon, ageal, iver, and cers and/or as under ve er preferred de benign disorders and
85:6342-6346 (1988); Flavell	Flavell as, for example, hyperplasia,	hyperplasia,

			Quant Biol 64:563-571 (1999);	Preferred indications include
			Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
			J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
			(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
			Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
			Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
			14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
			contents of each of which are	lymphoma, arthritis, AIDS,
			herein incorporated by	granulomatous disease,
			reference in its entirety. Mast	inflammatory bowel disease,
			cells that may be used	sepsis, neutropenia,
		-	according to these assays are	neutrophilia, psoriasis,
			publicly available (e.g.,	suppression of immune
			through the ATCC).	reactions to transplanted
		-	Exemplary human mast cells	organs and tissues, hemophilia,
			that may be used according to	hypercoagulation, diabetes
			these assays include the HMC-	mellitus, endocarditis,
			1 cell line, which is an	meningitis, and Lyme Disease.
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HODDN92	756	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the NFAT	include allergy, asthma, and
		through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
_		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and

production. Assays for the	inflammation and
activation of transcription	inflammatory disorders
through the Nuclear Factor of	Preferred indications also
Activated T cells (NFAT)	include blood disorders (e.g.,
response element are well-	as described below under
known in the art and may be	"Immune Activity", "Blood-
used or routinely modified to	Related Disorders", and/or
assess the ability of	"Cardiovascular Disorders").
polypeptides of the invention	Preferred indications include
(including antibodies and	autoimmune diseases (e.g.,
agonists or antagonists of the	rheumatoid arthritis, systemic
invention) to regulate NFAT	lupus erythematosis, multiple
transcription factors and	sclerosis and/or as described
modulate expression of genes	below) and
involved in	immunodeficiencies (e.g., as
immunomodulatory functions.	described below). Preferred
Exemplary assays for	indications include neoplastic
transcription through the	diseases (e.g., leukemia,
NFAT response element that	lymphoma, melanoma,
may be used or routinely	prostate, breast, lung, colon,
modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
(including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.

				85:6342-6346 (1988); De Boer	Preferred indications include
-				et al Int J Biochem Cell Biol	anemia nancytonenia
				31(10):1221-1236 (1999)· Ali	leukonenia thrombocytonenia
				et al J Immunol	lenkemias Hodokin's disease
				165(12):7215-7223 (2000):	acute lymphocytic anemia
				Hutchinson and McCloskey I	
				Hintoninson and McCloskey, J Biol Chem 270/27):16333	multiple myelome Burkitt's
				16338 (1005) and Turner et	lumbome arthritic AIDC
				of TExa Med 188:577-537	dynphoma, armins, AIDS,
				al., J Exp Med 188:32/-33/	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
		-		through the ATCC).	hypercoagulation, diabetes
-	-			Exemplary human mast cells	mellitus, endocarditis,
			·	that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HODDN92	756	Activation of	Kinase assay. JNK and p38	A highly preferred
			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly

	the art and may be used or		preferred embodiment of the
	routinely modified to assess		invention includes a method
	the ability of polypeptides of		for inhibiting endothelial cell
	the invention (including	-	growth. A highly preferred
	antibodies and agonists or		embodiment of the invention
-	antagonists of the invention) to		includes a method for
	promote or inhibit cell		stimulating endothelial cell
-	proliferation, activation, and		proliferation. An alternative
	apoptosis. Exemplary assays		highly preferred embodiment
	for JNK and p38 kinase		of the invention includes a
	activity that may be used or		method for inhibiting
	routinely modified to test JNK		endothelial cell proliferation.
	and p38 kinase-induced		A highly preferred
	activity of polypeptides of the		embodiment of the invention
	invention (including antibodies		includes a method for
	and agonists or antagonists of		stimulating apoptosis of
	the invention) include the		endothelial cells. An
	assays disclosed in Forrer et		alternative highly preferred
	al., Biol Chem 379(8-9):1101-		embodiment of the invention
	1110 (1998); Gupta et al., Exp	Exp	includes a method for
	Cell Res 247(2): 495-504		inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem		apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	·;	A highly preferred
	Chang and Karin, Nature		embodiment of the invention
-	410(6824):37-40 (2001); and		includes a method for
	Cobb MH, Prog Biophys Mol		stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);		endothelial cell activation. An
	the contents of each of which	ich	alternative highly preferred
	are herein incorporated by		embodiment of the invention
	reference in its entirety.		includes a method for
	Endothelial cells that may be		inhibiting (e.g., decreasing) the

avega eacht of militarooc beau	potition of and/on	_
 and any printing to the control of t	activation or deal all all	
are publicly available (e.g.,	macuvating endotherial cells.	
 through the ATCC).	A highly preferred	
Exemplary endothelial cells	embodiment of the invention	
that may be used according to	includes a method for	
these assays include human	stimulating angiogenisis. An	
 umbilical vein endothelial cells	alternative highly preferred	
 (HUVEC), which are	embodiment of the invention	-
endothelial cells which line	includes a method for	
venous blood vessels, and are	inhibiting angiogenesis. A	
involved in functions that	highly preferred embodiment	-
include, but are not limited to,	of the invention includes a	
angiogenesis, vascular	method for reducing cardiac	
permeability, vascular tone,	hypertrophy. An alternative	
and immune cell extravasation.	highly preferred embodiment	
	of the invention includes a	
	method for inducing cardiac	
	hypertrophy. Highly	
	preferred indications include	
	neoplastic diseases (e.g., as	
	described below under	
	"Hyperproliferative	
	Disorders"), and disorders of	
	the cardiovascular system	
 	(e.g., heart disease, congestive	
	heart failure, hypertension,	
	aortic stenosis,	
	cardiomyopathy, valvular	
	regurgitation, left ventricular	
	dysfunction, atherosclerosis	
	and atherosclerotic vascular	

ropathy,	rdiac	lial		ad, and/or	nder	rders").	cations	ar,	giogenic	nic	essels	itus, as	e vessels	fthe	eins	Highly	ons that	s and/or	. Highly	ons that	nd/or	_	cations	c activity		i"s	lisorders.	cations	d cancer,	coma,
disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,
disease,	intracar	hypertro	infarctic	hemody	as descr	"Cardio	Highly 1	include	endothe	disorder	disorder	such as	well as	themsel	arteries,	and/or I	preferre	stimulat	cardiova	preferre	inhibit	cardiova	Highly 1	include	to treat	leukemi	sarcoma	Highly 1	include	such as,
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		hemangioma (capillary and
		cavernous), glomus tumors,
		telangiectasia, bacillary
		angiomatosis,
		hemangioendothelioma,
		angiosarcoma,
		haemangiopericytoma,
		lymphangioma,
		lymphangiosarcoma. Highly
-		preferred indications also
		include cancers such as,
		prostate, breast, lung, colon,
		pancreatic, esophageal,
		stomach, brain, liver, and
		urinary cancer. Preferred
-		indications include benign
		dysproliferative disorders and
		pre-neoplastic conditions, such
		as, for example, hyperplasia,
		metaplasia, and/or dysplasia.
		Highly preferred indications
		also include arterial disease,
		such as, atherosclerosis,
		hypertension, coronary artery
		disease, inflammatory
		vasculitides, Reynaud"s
		disease and Reynaud"s
		phenomenom, aneurysms,
	-	restenosis; venous and
		lymphatic disorders such as
		thromhophlehitis

lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions),	implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis.	Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph	angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas

			heart disease, cardiac arrest,
			heart valve disease, and
			vascular disease.
			Preferred indications include
			blood disorders (e.g., as
			described below under
			"Immune Activity", "Blood-
			Related Disorders", and/or
			"Cardiovascular Disorders").
			Preferred indications include
			autoimmune diseases (e.g.,
			rheumatoid arthritis, systemic
			lupus erythematosis, multiple
			sclerosis and/or as described
			below) and
			immunodeficiencies (e.g., as
		ı	described below). Additional
			preferred indications include
			inflammation and
			inflammatory disorders (such
			as acute and chronic
			inflammatory diseases, e.g.,
			inflammatory bowel disease
			and Crohn's disease), and pain
			management.
757	Inhibition of	Reporter Assay: construct	
	squalene synthetase	contains regulatory and coding	
	gene transcription.	sequence of squalene	
		synthetase, the first specific	
		enzyme in the cholesterol	
		biosynthetic pathway. See	
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			Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the	
			contents of which are herein	
			incorporated by reference in its	
			entirety. Cells were treated	
			with SID supernatants, and	
			SEAP activity was measured	
			after 72 hours. HepG2 is a	
			human hepatocellular	
			carcinoma cell line (ATCC	
			HB-8065). See Knowles et al.,	
			Science. 209:497-9 (1980), the	
			contents of which are herein	
			incorporated by reference in its	
			entirety.	
HODFN71	757	IL-2 in Human T-		
		cell 293T		
HODFN71	757	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	highly preferred embodiment
			the ability of polypeptides of	of the invention includes a
			the invention (including	method for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth and upregulate the	Activity", "Blood-Related

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Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma
function of growth-related	genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety.	Human T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the JURKAT	cell line, which is a suspension	culture of leukemia cells that

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(e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic.	esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benion dysproliferative	disorders and pre-neoplastic	conditions, such as, for example, hyperplasia.	metaplasia, and/or dysplasia.	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication
produce IL-2 when stimulated.																								
																		-						

				disease as described below under "Infectious Disease").
HODFN71	757	SEAP in Molt4/SRE		
HODFN71	757	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include blood disorders (e.g.,
		through NFAT	Nuclear Factor of Activated T	as described below under
		response element in	cells (NFAT) response element	"Immune Activity", "Blood-
		immune cells (such	are well-known in the art and	Related Disorders", and/or
		as natural killer	may be used or routinely	"Cardiovascular Disorders").
		cells).	modified to assess the ability	Highly preferred indications
			of polypeptides of the	include autoimmune diseases
			invention (including antibodies	(e.g., rheumatoid arthritis,
			and agonists or antagonists of	systemic lupus erythematosis,
			the invention) to regulate	multiple sclerosis and/or as
			NFAT transcription factors and	described below),
			modulate expression of genes	immunodeficiencies (e.g., as
 			involved in	described below), boosting a T
			immunomodulatory functions.	cell-mediated immune
			Exemplary assays for	response, and suppressing a T
			transcription through the	cell-mediated immune
			NFAT response element that	response. Additional highly
			may be used or routinely	preferred indications include
			modified to test NFAT-	inflammation and
			response element activity of	inflammatory disorders. An
			polypeptides of the invention	additional highly preferred
			(including antibodies and	indication is infection (e.g., an
			agonists or antagonists of the	infectious disease as described
			invention) include assays	below under "Infectious
			disclosed in Berger et al., Gene	Disease"). Preferred

		66:1-10 (1998); Cullen and	indications include neoplastic
		Malm. Methods in Enzymol	diseases (e.g., leukemia,
		216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988);	"Hyperproliferative
		Aramburu et al., J Exp Med	Disorders"). Preferred
		182(3):801-810 (1995); De	indications include neoplasms
	-	Boer et al., Int J Biochem Cell	and cancers, such as, for
		Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
		Fraser et al., Eur J Immunol	and prostate, breast, lung,
-		29(3):838-844 (1999); and	colon, pancreatic, esophageal,
		Yeseen et al., J Biol Chem	stomach, brain, liver and
		268(19):14285-14293 (1993),	urinary cancer. Other preferred
		the contents of each of which	indications include benign
		are herein incorporated by	dysproliferative disorders and
		reference in its entirety. NK	pre-neoplastic conditions, such
		cells that may be used	as, for example, hyperplasia,
		according to these assays are	metaplasia, and/or dysplasia.
		publicly available (e.g.,	Preferred indications also
		through the ATCC).	include anemia, pancytopenia,
		Exemplary human NK cells	leukopenia, thrombocytopenia,
		that may be used according to	Hodgkin's disease, acute
		these assays include the NK-	lymphocytic anemia (ALL),
		YT cell line, which is a human	plasmacytomas, multiple
		natural killer cell line with	myeloma, Burkitt's lymphoma,
		cytolytic and cytotoxic	arthritis, AIDS, granulomatous
	-	activity.	disease, inflammatory bowel
			disease, sepsis, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted

				organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HODFN71	757	Activation of transcription	Assays for the activation of transcription through the	A preferred embodiment of the invention includes a
		through serum response element in	Serum Response Element (SRE) are well-known in the	method for inhibiting (e.g., reducing) TNF alpha
		immune cells (such as natural killer	art and may be used or routinely modified to assess	production. An alternative highly preferred embodiment
		cells).	the ability of polypeptides of	of the invention includes a method for stimulating (e.g
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth and upregulate the	Activity", "Blood-Related
			function of growth-related	Disorders", and/or
			genes in many cell types.	"Cardiovascular Disorders"),
			Exemplary assays for	Highly preferred indications
			transcription through the SRE	include autoimmune diseases
			that may be used or routinely	(e.g., rheumatoid arthritis,
			modified to test SRE activity	systemic lupus erythematosis,
			of the polypeptides of the	Crohn"s disease, multiple
			invention (including antibodies	sclerosis and/or as described
			and agonists or antagonists of	below), immunodeficiencies
			the invention) include assays	(e.g., as described below),
			disclosed in Berger et al., Gene	boosting a T cell-mediated
			66:1-10 (1998); Cullen and	immune response, and

suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and	inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly	preferred indication is sepsis. Highly preferred indications include neoplastic diseases	and/or as described below under "Hyperproliferative Disorders"). Additionally,	highly preferred indications include neoplasms and	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid	tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of	which are herein incorporated by reference in its entirety. T cells that may be used	account to these assays are publicly available (e.g., through the ATCC).	used according to these assays include the NK-YT cell line, which is a human natural killer	cell line with cytolytic and cytotoxic activity.			
			=					

Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, incutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectiou (e.g., an infectious disease as described below under "Infectious Disease").		A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention
		Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of
	SEAP in NK16/STAT6	Activation of transcription through CD28 response element in immune cells (such as T-cells).
	757	757
	HODFN71	HODFN71

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includes a method for	inhibiting T cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	activating T cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting the activation of	and/or inactivating T cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	IL-2 production. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting (e.g.,	reducing) IL-2 production.	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	imminodeficiencies (e.g., as
polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to stimulate IL-2	expression in T cells.	Exemplary assays for	transcription through the CD28	response element that may be	used or routinely modified to	test CD28-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	McGuire and Iacobelli, J	Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	3(1):552-560 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are
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	publicly available (e.g.,	described below), boosting a T
	through the ATCC).	cell-mediated immune
	Exemplary human T cells that	response, and suppressing a T
	may be used according to these	cell-mediated immune
	assays include the SUPT cell	response. Highly preferred
	line, which is a suspension	indications include neoplastic
	culture of IL-2 and IL-4	diseases (e.g., melanoma, renal
	responsive T cells.	cell carcinoma, leukemia,
		lymphoma, and/or as described
		below under
		"Hyperproliferative
		Disorders"). Highly preferred
		indications include neoplasms
		and cancers, such as, for
		example, melanoma (e.g.,
		metastatic melanoma), renal
		cell carcinoma (e.g., metastatic
		renal cell carcinoma),
		leukemia, lymphoma (e.g., T
		cell lymphoma), and prostate,
		breast, lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
-		example, hyperplasia,
		metaplasia, and/or dysplasia.
		A highly preferred indication
		includes infection (e.g.,

			AIDS tuberculosis infections
			second with annulamental
	-		associated with granuloinatous
			disease, and osteoporosis,
			and/or as described below
			under "Infectious Disease"). A
			highly preferred indication is
			AIDS. Additional highly
			preferred indications include
			suppression of immune
			reactions to transplanted
			organs and/or tissues, uveitis,
			psoriasis, and tropical spastic
			paraparesis. Preferred
			indications include blood
			disorders (e.g., as described
			below under "Immune
			Activity", "Blood-Related
			Disorders", and/or
			"Cardiovascular Disorders").
			Preferred indications also
			include anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
_			myeloma, Burkitt's lymphoma,
			arthritis, granulomatous
			disease, inflammatory bowel
			disease, sepsis, neutropenia,
			neutrophilia, hemophilia,
			hypercoagulation, diabetes

				mellitus, endocarditis, meningitis, Lyme Disease,
HODFN71	757	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include inflammation and
		through NFKB	NFKB response element are	inflammatory disorders.
		response element in	well-known in the art and may	Highly preferred indications
		immune cells (such	be used or routinely modified	include blood disorders (e.g.,
		as T-cells).	to assess the ability of	as described below under
			polypeptides of the invention	"Immune Activity", "Blood-
			including antibodies and	Related Disorders", and/or
			agonists or antagonists of the	"Cardiovascular Disorders").
			invention) to regulate NFKB	Highly preferred indications
			transcription factors and	include autoimmune diseases
			modulate expression of	(e.g., rheumatoid arthritis,
			immunomodulatory genes.	systemic lupus erythematosis,
			Exemplary assays for	multiple sclerosis and/or as
			transcription through the	described below), and
	-		NFKB response element that	immunodeficiencies (e.g., as
			may be used or rountinely	described below). An
			modified to test NFKB-	additional highly preferred
			response element activity of	indication is infection (e.g.,
			polypeptides of the invention	AIDS, and/or an infectious
			(including antibodies and	disease as described below
			agonists or antagonists of the	under "Infectious Disease").
			invention) include assays	Highly preferred indications
 			disclosed in Berger et al., Gene	include neoplastic diseases
-			66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
			Malm, Methods in Enzymol	lymphoma, and/or as described
			216:362-368 (1992); Henthorn	below under
			et al., Proc Natl Acad Sci USA	"Hyperproliferative

				reactions to transplanted
				organs, asthma and allergy.
HODGE68	758	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	highly preferred embodiment
		`	the ability of polypeptides of	of the invention includes a
			the invention (including	method for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
_			in growth and upregulate the	Activity", "Blood-Related
			function of growth-related	Disorders", and/or
-			genes in many cell types.	"Cardiovascular Disorders"),
			Exemplary assays for	Highly preferred indications
			transcription through the SRE	include autoimmune diseases
			that may be used or routinely	(e.g., rheumatoid arthritis,
			modified to test SRE activity	systemic lupus erythematosis,
			of the polypeptides of the	Crohn"s disease, multiple
			invention (including antibodies	sclerosis and/or as described
			and agonists or antagonists of	below), immunodeficiencies
		-	the invention) include assays	(e.g., as described below),
			disclosed in Berger et al., Gene	boosting a T cell-mediated
			66:1-10 (1998); Cullen and	immune response, and
			Malm, Methods in Enzymol	suppressing a T cell-mediated
			216:362-368 (1992); Henthorn	immune response. Additional
			et al., Proc Natl Acad Sci USA	highly preferred indications

include inflammation and inflammatory disorders, and treating joint damage in	arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,	highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma	tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute
85:6342-6346 (1988); Benson incet al., J Immunol 153(9):3862- inf 3873 (1994); and Black et al., tre			assays include the JURKAT include the JURKAT include the JURKAT include the JURKAT cell line, which is a suspension can culture of leukemia cells that lyngalized for the suspension can contain the line of leukemia cells that lyngalized for the suspension can be supplied that lyngalized for the suspension contains the		pre ber	exi me Pre and and leu Ho
85:6. et al. 3873	viru (1997) whic by re	used are p through through through through through the contract of the contrac	may assay cell l			
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759 Production of MIP-1alpha FMAT. Assays MIP1alpha for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel. disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Assays A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. ge and T An alternative highly preferred embodiment of the invention may be includes a method for includes a method for includes a method for includes a method for may be includes a method for includes a method for includes a method for An alternative highly preferred embodiment of the invention may be includes a method for MIP1a production. A highly
(including antibodies and	
agonists or antagonists of the	sts of the disease as described below

			(1997); and Nardelli et al., J	organs and tissues, hemophilia,
			Leukoc Biol 65:822-828	hypercoagulation, diabetes
			(1999), the contents of each of	mellitus, endocarditis,
			which are herein incorporated	meningitis, Lyme Disease,
			by reference in its entirety.	asthma, and allergy.
			Human dendritic cells that may	Preferred indications also
			be used according to these	include neoplastic diseases
			assays may be isolated using	(e.g., leukemia, lymphoma,
			techniques disclosed herein or	and/or as described below
			otherwise known in the art.	under "Hyperproliferative
			Human dendritic cells are	Disorders"). Highly preferred
			antigen presenting cells in	indications include neoplasms
			suspension culture, which,	and cancers, such as, leukemia,
			when activated by antigen	lymphoma, prostate, breast,
			and/or cytokines, initiate and	lung, colon, pancreatic,
			upregulate T cell proliferation	esophageal, stomach, brain,
			and functional activities.	liver, and urinary cancer. Other
				preferred indications include
				benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
HOEDB32	759	Production of TNF	TNFa FMAT. Assays for	A highly preferred
		alpha by dendritic	immunomodulatory proteins	embodiment of the invention
		cells	produced by activated	includes a method for
			macrophages, T cells,	inhibiting (e.g., decreasing)
			fibroblasts, smooth muscle,	TNF alpha production. An
			and other cell types that exert a	alternative highly preferred
			wide variety of inflammatory	embodiment of the invention
			and cytotoxic effects on a	includes a method for

		variety of cells are well known	stimulating (e.g., increasing)
-	50.	in the art and may be used or	TNF alpha production.
		routinely modified to assess	Highly preferred indications
		the ability of polypeptides of	include blood disorders (e.g.,
		the invention (including	as described below under
		antibodies and agonists or	"Immune Activity", "Blood-
		antagonists of the invention) to	Related Disorders", and/or
		mediate immunomodulation,	"Cardiovascular Disorders"),
		modulate inflammation and	Highly preferred indications
		cytotoxicity. Exemplary	include autoimmune diseases
		assays that test for	(e.g., rheumatoid arthritis,
		immunomodulatory proteins	systemic lupus erythematosis,
		evaluate the production of	Crohn"s disease, multiple
		cytokines such as tumor	sclerosis and/or as described
		necrosis factor alpha (TNFa),	below), immunodeficiencies
		and the induction or inhibition	(e.g., as described below),
		of an inflammatory or	boosting a T cell-mediated
		cytotoxic response. Such	immune response, and
		assays that may be used or	suppressing a T cell-mediated
		routinely modified to test	immune response. Additional
		immunomodulatory activity of	highly preferred indications
		polypeptides of the invention	include inflammation and
		(including antibodies and	inflammatory disorders, and
		agonists or antagonists of the	treating joint damage in
		invention) include assays	patients with rheumatoid
		disclosed in Miraglia et al., J	arthritis. An additional highly
		Biomolecular Screening 4:193-	preferred indication is sepsis.
		204(1999); Rowland et al.,	Highly preferred indications
		"Lymphocytes: a practical	include neoplastic diseases
		approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
		(2000); Verhasselt et al., Eur J	and/or as described below

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under "Hyperproliferative Disorders"). Additionally,	highly preferred indications include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues.
Immunol 28(11):3886-3890 (1198); Dahlen et al., J	Immunol 160(7):3585-3593 (1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.									
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hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		A preferred embodiment of	the invention includes a	method for inhibiting (e.g.,	reducing) TNF alpha	production. An alternative	highly preferred embodiment	of the invention includes a	method for stimulating (e.g.,	increasing) TNF alpha		indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple
		Assays for the activation of	transcription through the	Serum Response Element	(SRE) are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate serum response	factors and modulate the	expression of genes involved	in growth and upregulate the	function of growth-related	genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the
	MCP-1 in Eol-1	Activation of	transcription	through serum	response element in	immune cells (such	as natural killer	cells).														
	759	759																				
	HOEDB32	HOEDB32		_			_			-												

sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and	treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below		melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include
invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998): Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., Imminol 153(9):3862-	3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated	by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g.,	through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and	cytotoxic activity.
		<u>-</u> .			

benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication	is infection (e.g., an infectious	disease as described below	under "Infectious Disease").	ivation of A highly preferred	ugh the indication is allergy.	rs and Another highly preferred
																												Assays for the activation of	transcription through the	Signal Transducers and
																												Activation of	transcription	through STAT6
																												759		
																												HOEDB32		

response element in	Activators of Transcription	indication is asthma.
 immune cells (such	(STAT6) response element are	Additional highly preferred
as T-cells).	well-known in the art and may	indications include
	be used or routinely modified	inflammation and
	to assess the ability of	inflammatory disorders.
	polypeptides of the invention	Preferred indications include
	(including antibodies and	blood disorders (e.g., as
	agonists or antagonists of the	described below under
 	invention) to regulate STAT6	"Immune Activity", "Blood-
	transcription factors and	Related Disorders", and/or
	modulate the expression of	"Cardiovascular Disorders").
	multiple genes. Exemplary	Preferred indications include
	assays for transcription	autoimmune diseases (e.g.,
	through the STAT6 response	rheumatoid arthritis, systemic
	element that may be used or	lupus erythematosis, multiple
	routinely modified to test	sclerosis and/or as described
	STAT6 response element	below) and
	activity of the polypeptides of	immunodeficiencies (e.g., as
	the invention (including	described below).
	antibodies and agonists or	Preferred indications include
	antagonists of the invention)	neoplastic diseases (e.g.,
	include assays disclosed in	leukemia, lymphoma,
	Berger et al., Gene 66:1-10	melanoma, and/or as described
	(1998); Cullen and Malm,	below under
	Methods in Enzymol 216:362-	"Hyperproliferative
	368 (1992); Henthorn et al.,	Disorders"). Preferred
	Proc Natl Acad Sci USA	indications include neoplasms
	85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
	et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
	(1998); Moffatt et al.,	prostate, breast, lung, colon,
	Transplantation 69(7):1521-	pancreatic, esophageal,

				1523 (2000); Curiel et al., Eur	stomach, brain, liver and
				J Immunol 27(8):1982-1987	urinary cancer. Other preferred
				(1997); and Masuda et al., J	indications include benign
				Biol Chem 275(38):29331-	dysproliferative disorders and
				29337 (2000), the contents of	pre-neoplastic conditions, such
				each of which are herein	as, for example, hyperplasia,
				incorporated by reference in its	metaplasia, and/or dysplasia.
-				entirety. T cells that may be	Preferred indications include
				used according to these assays	anemia, pancytopenia,
				are publicly available (e.g.,	leukopenia, thrombocytopenia,
				through the ATCC).	Hodgkin's disease, acute
				Exemplary T cells that may be	lymphocytic anemia (ALL),
				used according to these assays	plasmacytomas, multiple
				include the SUPT cell line,	myeloma, Burkitt's lymphoma,
				which is a suspension culture	arthritis, AIDS, granulomatous
				of IL-2 and IL-4 responsive T	disease, inflammatory bowel
				cells.	disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additional preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	НОҒМQ33	760	Regulation of viability and	Assays for the regulation of viability and proliferation of	A highly preferred indication is diabetes mellitus. An
			viacinty and	the man brother and brother and the same and	

	proliferation of	cells in vitro are well-known in	additional highly preferred
	pancreatic beta	the art and may be used or	
	cells.	routinely modified to assess	associated with diabetes (e.g.,
		the ability of polypeptides of	diabetic retinopathy, diabetic
		the invention (including	nephropathy, kidney disease
		antibodies and agonists or	(e.g., renal failure,
		antagonists of the invention) to	nephropathy and/or other
		regulate viability and	diseases and disorders as
		proliferation of pancreatic beta	described in the "Renal
	-	cells. For example, the Cell	Disorders" section below),
		Titer-Glo luminescent cell	diabetic neuropathy, nerve
		viability assay measures the	disease and nerve damage
		number of viable cells in	(e.g., due to diabetic
		culture based on quantitation	neuropathy), blood vessel
-		of the ATP present which	blockage, heart disease, stroke,
		signals the presence of	impotence (e.g., due to diabetic
		metabolically active cells.	neuropathy or blood vessel
		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
		test regulation of viability and	nonketotic hyperglycemic-
		proliferation of pancreatic beta	hyperosmolar coma,
		cells by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Ohtani KI, et al.,	diseases and disorders as
		Endocrinology, 139(1):172-8	described in the
		(1998); Krautheim A, et al,	"Cardiovascular Disorders"
		Exp Clin Endocrinol Diabetes,	section below), dyslipidemia,
		107 (1):29-34 (1999), the	endocrine disorders (as
		contents of each of which is	described in the "Endocrine

				herein incorporated by	Disorders" section below),
				reference in its entirety.	neuropathy, vision impairment
				Pancreatic cells that may be	(e.g., diabetic retinopathy and
				used according to these assays	blindness), ulcers and impaired
				are publicly available (e.g.,	wound healing, and infection
				through the ATCC) and/or	(e.g., infectious diseases and
	•			may be routinely generated.	disorders as described in the
				Exemplary pancreatic cells that	"Infectious Diseases" section
				may be used according to these	below, especially of the
				assays include HITT15 Cells.	urinary tract and skin), carpal
				HITT15 are an adherent	tunnel syndrome and
				epithelial cell line established	Dupuytren's contracture). An
			-	from Syrian hamster islet cells	additional highly preferred
				transformed with SV40. These	indication is obesity and/or
				cells express glucagon,	complications associated with
				somatostatin, and	obesity. Additional highly
				glucocorticoid receptors. The	preferred indications include
				cells secrete insulin, which is	weight loss or alternatively,
				stimulated by glucose and	weight gain. Additional highly
				glucagon and suppressed by	preferred indications are
				somatostatin or	complications associated with
				glucocorticoids. ATTC# CRL-	insulin resistance.
				1777 Refs: Lord and	
				Ashcroft. Biochem. J. 219:	
<u>.</u>				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
				4339-4343, 1981.	
	НОҒМQ33	092	SEAP in Molt4/SRE		
	HOFMT75	761	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as

	Signaling Pathway.	transduction that regulate cell	described below under
		proliferation, activation, or	"Hyperproliferative
		apoptosis are well known in	Disorders"), blood disorders
		the art and may be used or	(e.g., as described below under
		routinely modified to assess	"Immune Activity",
_		the ability of polypeptides of	"Cardiovascular Disorders",
		the invention (including	and/or "Blood-Related
		antibodies and agonists or	Disorders"), and infection
		antagonists of the invention) to	(e.g., an infectious disease as
		promote or inhibit immune cell	described below under
-		(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
		activation, and apoptosis.	preferred indications include
		Exemplary assays for JNK and	autoimmune diseases (e.g.,
		p38 kinase activity that may be	rheumatoid arthritis, systemic
-		used or routinely modified to	lupus erythematosis, multiple
		test JNK and p38 kinase-	sclerosis and/or as described
-		induced activity of	below) and
		polypeptides of the invention	immunodeficiencies (e.g., as
		(including antibodies and	described below). Additional
		agonists or antagonists of the	highly preferred indications
-		invention) include the assays	include inflammation and
		disclosed in Forrer et al., Biol	inflammatory disorders.
		Chem 379(8-9):1101-1110	Highly preferred indications
		(1998); Gupta et al., Exp Cell	also include neoplastic
		Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
		Kyriakis JM, Biochem Soc	lymphoma, and/or as described
		Symp 64:29-48 (1999); Chang	below under
		and Karin, Nature	"Hyperproliferative
		410(6824):37-40 (2001); and	Disorders"). Highly preferred
		Cobb MH, Prog Biophys Mol	indications include neoplasms
		Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,

				the contents of each of which	lymphoma, prostate, breast.
				are herein incorporated by	lung, colon, pancreatic,
				reference in its entirety. T	esophageal, stomach, brain,
_				cells that may be used	liver, and urinary cancer. Other
				according to these assays are	preferred indications include
				publicly available (e.g.,	benign dysproliferative
				through the ATCC).	disorders and pre-neoplastic
				Exemplary mouse T cells that	conditions, such as, for
				may be used according to these	example, hyperplasia,
				assays include the CTLL cell	metaplasia, and/or dysplasia.
				line, which is an IL-2	Preferred indications include
				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
				activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
	_				plasmacytomas, multiple
					myeloma, Burkitt"s lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
				1000	meningitis, and Lyme Disease.
	HOFMT75	761	Activation of	Kinase assay. JNK and p38	A highly preferred
			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
				the art and may be used or	preferred embodiment of the

invention includes a method for inhibiting endothelial cell growth. A highly preferred	embodiment of the invention includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing) the	activation of and/or
routinely modified to assess the ability of polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) to	promote or inhibit cell	proliferation, activation, and	apoptosis. Exemplary assays for INK and n38 kinase	activity that may be used or	routinely modified to test JNK	and p38 kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays
			_																							

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inactivating endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease diabetic nenhronathy
are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																	
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cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma,	haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications	also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis,

lymphedema; and other	vascular disorders such as	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,

				heart valve disease, and
				vascular disease.
				Preferred indications include
				blood disorders (e.g., as
				described below under
				"Immune Activity", "Blood-
				Related Disorders", and/or
				"Cardiovascular Disorders").
				Preferred indications include
				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
				described below). Additional
				preferred indications include
				inflammation and
				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HOFNY91	762	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method

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	the invention (including	tor stimulating (e.g.,
	antibodies and agonists or	increasing) TNF alpha
	antagonists of the invention) to	production. Preferred
	regulate the serum response	indications include blood
	factors and modulate the	disorders (e.g., as described
	expression of genes involved	below under "Immune
	in growth. Exemplary assays	Activity", "Blood-Related
	for transcription through the	Disorders", and/or
	SRE that may be used or	"Cardiovascular Disorders"),
	routinely modified to test SRE	Highly preferred indications
	activity of the polypeptides of	include autoimmune diseases
	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
	antagonists of the invention)	Crohn"s disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
-	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
	cells that may be used	arthritis. An additional highly
-	according to these assays are	preferred indication is sepsis.
	publicly available (e.g.,	Highly preferred indications
	through the ATCC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,

		may be used according to these	and/or as described below
		assays include the CTLL cell	under "Hyperproliferative
		line, which is an IL-2	Disorders"). Additionally,
		dependent suspension culture	highly preferred indications
		of T cells with cytotoxic	include neoplasms and
		activity.	cancers, such as, for example,
			leukemia, lymphoma,
			melanoma, glioma (e.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
	 -		myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune

reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" and/or "Cardiovascular Disorders"). Highly preferred indications include neoplasms and cancers such as, for
	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
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	HOFNY91

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example, leukemia, lymphoma, melanoma, renal cell carcinoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of muscle (such as, rhabdomyoma, and rhabdosarcoma), cardiovascular disorders (such as congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve
mia, ly al cell proste lon, pe lon, pe mach, y canc trions re-neo h as, fe plasia, lor dy	s, myc s, myc sphy, c s, and), disord disord disord cart fa iovasc heart ch
leuker a, reng a, reng a, and ng, co al, sto al, sto and p and p ss, such hyper hyper ia, and	referre iabete ell atro such as yoma, rcoma scular stive h myxc al card lities, l
example, leukemia, lymp melanoma, renal cell carcinoma, and prostate, breast, lung, colon, panci esophageal, stomach, bri liver and urinary cancer. preferred indications incl benign dysproliferative disorders and pre-neopla conditions, such as, for example, hyperplasia, metaplasia, and/or dyspla	Highly preferred indication include diabetes, myopathy muscle cell atrophy, cancer muscle (such as, rhabdomyoma, and rhabdosarcoma), cardiovascular disorders (sa so congestive heart failure, cachexia, myxomas, fibron congenital cardiovascular abnormalities, heart disease cardiac arrest, heart valve
extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit myoblast cell proliferation. Exemplary assays for myoblast cell proliferation that may be used
extravasation. Exemplary endothelial cells that may be used according to these assay include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from bloo vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) tstimulate or inhibit myoblast cell proliferation. Exemplary assays for myoblast cell proliferation that may be used
extravasation. Exemplendothelial cells that maused according to these include human umbilicated the manubilicated that are available from commercial sources. The expression of VCAM (CD106), a membraneassociated protein, can lupregulated by cytoking other factors, and contript to the extravasation of lymphocytes, leucocyte other immune cells from vessels; thus VCAM expression plays a role promoting immune and inflammatory responses	Assays for muscle cell proliferation are well k the art and may be use routinely modified to the ability of polypeptithe invention (includin antibodies and agonist antagonists of the investimulate or inhibit mycell proliferation. Exe assays for myoblast ce proliferation that may
vasatii thelial accorr de hu thelial h are a nercia ession (106), a siated gulated gulated e extra hocyte immu- els; thu	ys for feration rt and nely molity on the properties of the proper
extra endo used inclu endo whic comi expra (CD) assoc upre; other to the lymp other vesss expra expra infla	Assa proli the a routi the i the i antia antia stim cell j assa; proli
	st cell
	Myoblast cell proliferation
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disease, vascular disease, and also as described below under "Cardiovascular Disorders"), stimulating myoblast	proliferation, and inhibiting myoblast proliferation.
or routinely modified to test activity of polypeptides and antibodies of the invention (including agonists or	antagonists of the invention) include, for example, assays disclosed in: Soeta, C., et al. "Possible role for the c-ski gene in the proliferation of myogenic cells in regenerating skeletal muscles of rats" Dev Growth Differ Apr;43(2):155-64 (2001); Ewton DZ, et al., "IGF binding proteins-4, -5 and -6 may play specialized roles during L6 myoblast proliferation and differentiation." J Endocrinol Mar;144(3):539-53 (1995); and, Pampusch MS, et al., "Effect of transforming growth factor beta on proliferation of L6 and embryonic porcine myogenic cells." J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these

st 5 n		A highly preferred			stimulating endothelial cell	growth. An alternative highly	preferred embodiment of the	invention includes a method		growth. A highly preferred	embodiment of the invention	to includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	K endothelial cell proliferation.	A highly preferred	
assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.		Kinase assay. JNK and p38	kinase assays for signal	transduction that regulate cell	proliferation, activation, or	apoptosis are well known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	promote or inhibit cell	proliferation, activation, and	apoptosis. Exemplary assays	for JNK and p38 kinase	activity that may be used or	routinely modified to test JNK	and p38 kinase-induced	activity of polypeptides of the
·	Caspase (+camptothecin) in SW480	Activation of	Endothelial Cell	p38 or JNK	Signaling Pathway.															
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	H0F0C73	HOGAW62		_																
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			invention (including antibodies	includes a method for
			and agonists or antagonists of	stimulating apoptosis of
			the invention) include the	endothelial cells. An
			assays disclosed in Forrer et	alternative highly preferred
			al., Biol Chem 379(8-9):1101-	embodiment of the invention
			1110 (1998); Gupta et al., Exp	includes a method for
			Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
			(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
-			Soc Symp 64:29-48 (1999);	A highly preferred
			Chang and Karin, Nature	embodiment of the invention
			410(6824):37-40 (2001); and	includes a method for
			Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
			Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	•		the contents of each of which	alternative highly preferred
			are herein incorporated by	embodiment of the invention
			reference in its entirety.	includes a method for
			Endothelial cells that may be	inhibiting (e.g., decreasing) the
			used according to these assays	activation of and/or
			are publicly available (e.g.,	inactivating endothelial cells.
			through the ATCC).	A highly preferred
			Exemplary endothelial cells	embodiment of the invention
			that may be used according to	includes a method for
			these assays include human	stimulating angiogenisis. An
_			umbilical vein endothelial cells	alternative highly preferred
		-	(HUVEC), which are	embodiment of the invention
			endothelial cells which line	includes a method for
			venous blood vessels, and are	inhibiting angiogenesis. A
			involved in functions that	highly preferred embodiment
			include, but are not limited to,	of the invention includes a
			angiogenesis, vascular	method for reducing cardiac
	*		permeability, vascular tone,	hypertrophy. An alternative

and immune cell extravasation.
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themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that	stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications	include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications	include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis,	hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and

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		urinary cancer. Preferred
		. 1' .'
		indications include benign
		dysproliferative disorders and
		pre-neoplastic conditions, such
		as, for example, hyperplasia,
		metaplasia, and/or dysplasia.
		Highly preferred indications
		also include arterial disease,
	 	such as, atherosclerosis,
		hypertension, coronary artery
		disease, inflammatory
		vasculitides, Reynaud"s
		disease and Reynaud"s
		phenomenom, aneurysms,
		restenosis; venous and
		lymphatic disorders such as
		thrombophlebitis,
-		lymphangitis, and
		lymphedema; and other
		vascular disorders such as
		peripheral vascular disease,
		and cancer. Highly
		preferred indications also
		include trauma such as
-		wounds, burns, and injured
		tissue (e.g., vascular injury
		such as, injury resulting from
		balloon angioplasty, and
		atheroschlerotic lesions),
		implant fixation, scarring,
		ischemia reperfusion injury,

rheumatoid arthritis, cerebrovascular disease, renal	diseases such as acute renal failure, and osteoporosis.	Additional highly preferred	indications include stroke, graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described

below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or
	Activation of transcription through serum response element in immune cells (such as T-cells).
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				nreferred indications include
				1: 1:1:
				benign dysproliterative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
-				suppression of immune
				reactions to transplanted
-				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
	•			cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
H0QBJ82	766	Inhibition of	Reporter Assay: construct	
		squalene synthetase	contains regulatory and coding	

	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),
sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies.
gene transcription.	Insulin Secretion
	992
	HOQBJ82

Insulin secretion from	diabetic neuropathy, nerve
pancreatic beta cells is	disease and nerve damage
upregulated by glucose and	(e.g., due to diabetic
also by certain	neuropathy), blood vessel
proteins/peptides, and	blockage, heart disease, stroke,
disregulation is a key	impotence (e.g., due to diabetic
component in diabetes.	neuropathy or blood vessel
Exemplary assays that may be	blockage), seizures, mental
used or routinely modified to	confusion, drowsiness,
test for stimulation of insulin	nonketotic hyperglycemic-
 secretion (from pancreatic	hyperosmolar coma,
cells) by polypeptides of the	cardiovascular disease (e.g.,
invention (including antibodies	heart disease, atherosclerosis,
 and agonists or antagonists of	microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Shimizu, H., et	diseases and disorders as
al., Endocr J, 47(3):261-9	described in the
(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
17 (1999); Filipsson, K., et al.,	endocrine disorders (as
Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
(1998); Olson, L.K., et al., J	Disorders" section below),
Biol Chem, 271(28):16544-52	neuropathy, vision impairment
(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
Journal of Biomolecular	blindness), ulcers and impaired
Screening, 4:193-204 (1999),	wound healing, and infection
the contents of each of which	(e.g., infectious diseases and
is herein incorporated by	disorders as described in the
reference in its entirety.	"Infectious Diseases" section
Pancreatic cells that may be	below, especially of the
used according to these assays	urinary tract and skin), carpal

			are publicly available (e.g.,	tunnel syndrome and
		,	through the ATCC) and/or	Dupuytren's contracture).
		-	may be routinely generated.	An additional highly preferred
			Exemplary pancreatic cells that	indication is obesity and/or
			may be used according to these	complications associated with
			assays include HITT15 Cells.	obesity. Additional highly
			HITT15 are an adherent	preferred indications include
			epithelial cell line established	weight loss or alternatively,
			from Syrian hamster islet cells	weight gain. Additional highly
			transformed with SV40. These	preferred indications are
			cells express glucagon,	complications associated with
			somatostatin, and	insulin resistance.
			glucocorticoid receptors. The	
			cells secrete insulin, which is	
			stimulated by glucose and	
			glucagon and suppressed by	
			somatostatin or	
			glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
			4339-4343, 1981.	
HOSBY40	191	Regulation of	Assays for the regulation of	A highly preferred
		transcription	transcription through the FAS	indication is diabetes mellitus.
		through the FAS	promoter element are well-	An additional highly preferred
		promoter element	known in the art and may be	indication is a complication
		in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
			assess the ability of	diabetic retinopathy, diabetic
			polypeptides of the invention	nephropathy, kidney disease
			(including antibodies and	(e.g., renal failure,

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nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e a infections diseases and
agonists or antagonists of the	invention) to activate the FAS	promoter element in a reporter	construct and to regulate	transcription of FAS, a key	enzyme for lipogenesis. FAS	promoter is regulated by many	transcription factors including	SREBP. Insulin increases FAS	gene transcription in livers of	diabetic mice. This	stimulation of transcription is	also somewhat glucose	dependent. Exemplary assays	that may be used or routinely	modified to test for FAS	promoter element activity (in	hepatocytes) by polypeptides	of the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Xiong, S., et al., Proc Natl	Acad Sci U.S.A., 97(8):3948-	53 (2000); Roder, K., et al.,	Eur J Biochem, 260(3):743-51	(1999); Oskouian B, et al.,	Biochem J, 317 (Pt 1):257-65	(1996); Berger, et al., Gene	66:1-10 (1988); and, Cullen,	B. et al., Methods in Enzymol le g infections diseases and
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contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays, such available (e.g., through the routinely generated. ATCC) and/or may be used available (e.g., through the routinely generated. ATCC) and/or may be used available to used according to these weight loss or alternatively, assays include rat liver weight gain. Aditional highly preferred indications are complications associated with insulin, or cAMP derivatives.	Assays for measuring Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention detection, diagnosis, prevention, and/or treatment of Vascular Disease, invention) to regulate ICAM-1 Atherosclerosis, Restenosis, that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in Rolfe RE et al
216:362 contents herein is reference Hepatoca accordin as H4III availabl ATCC) routinel Exempl may be assays is hepaton with gh	Production of Assays ICAM-1 express well-kn be used to asses polyper (includi agonists inventic express that ma modifie
	767 SE 768 Pr 1C
	HOSBY40 HOSDJ25

				Atherosclerosis, 149(1):99-110 (2000): Panettieri RA Jr. et al	
-				J Immunol, 154(5):2358-2365	
				(1995); and, Grunstein MM, et	
				al., Am J Physiol Lung Cell	
	•			Mol Physiol, 278(6):L1154-	
				L1163 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
				used according to these assays	
				are publicly available (e.g.,	
				through the ATCC) and/or	
				may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include Aortic Smooth Muscle	
				Cells (AOSMC); such as	
				bovine AOSMC.	
	HOSDJ25	768	SEAP in HIB/CRE		
	HOSDJ25	892	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
			cells).	modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as

	NEAT	NFAT transcription factors and	decompad helon)
	··		described below),
	Inpom	modulate expression of genes	immunodeficiencies (e.g., as
	involved in	ed in	described below), boosting a T
-	immur	immunomodulatory functions.	cell-mediated immune
	Exemi	Exemplary assays for	response, and suppressing a T
	transcr	transcription through the	cell-mediated immune
	NFAT	NFAT response element that	response. Additional highly
	may be	may be used or routinely	preferred indications include
	modifi	modified to test NFAT-	inflammation and
	respon	response element activity of	inflammatory disorders. An
	polype	polypeptides of the invention	additional highly preferred
	(includ	(including antibodies and	indication is infection (e.g., an
	agonis	agonists or antagonists of the	infectious disease as described
	inventi	invention) include assays	below under "Infectious
	disclos	disclosed in Berger et al., Gene	Disease"). Preferred
	66:1-1	66:1-10 (1998); Cullen and	indications include neoplastic
	Malm,	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:36	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., I	et al., Proc Natl Acad Sci USA	below under
-	85:634	85:6342-6346 (1988);	"Hyperproliferative
	Aramb	Aramburu et al., J Exp Med	Disorders"). Preferred
	182(3)	182(3):801-810 (1995); De	indications include neoplasms
	Boer e	Boer et al., Int J Biochem Cell	and cancers, such as, for
	Biol 33	Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
	Fraser	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):8	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseer	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the cor	the contents of each of which	indications include benign
	are her	are herein incorporated by	dysproliferative disorders and
	referen	reference in its entirety. NK	pre-neoplastic conditions, such

				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human NK cells	leukopenia, thrombocytopenia,
				that may be used according to	Hodgkin's disease, acute
				these assays include the NK-	lymphocytic anemia (ALL),
				YT cell line, which is a human	plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
_					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HOSDJ25	768	Regulation of	Caspase Apoptosis. Assays	A highly preferred
			apoptosis in	for caspase apoptosis are well	indication is diabetes mellitus.
			pancreatic beta	known in the art and may be	An additional highly preferred
			cells.	used or routinely modified to	indication is a complication
				assess the ability of	associated with diabetes (e.g.,
				polypeptides of the invention	diabetic retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to promote caspase	nephropathy and/or other
				protease-mediated apoptosis.	diseases and disorders as
				Apoptosis in pancreatic beta is	described in the "Renal

	bas acitathai dita betsioosse	on and	Disorders" section helow)
	progression of diabetes.	3.	diabetic neuropathy, nerve
	Exemplary assays for caspase	caspase	disease and nerve damage
	apoptosis that may be used or	used or	(e.g., due to diabetic
	routinely modified to test	est	neuropathy), blood vessel
	capase apoptosis activity of	ity of	blockage, heart disease, stroke,
	polypeptides of the invention	ention	impotence (e.g., due to diabetic
	(including antibodies and	pun	neuropathy or blood vessel
	agonists or antagonists of the	of the	blockage), seizures, mental
	invention) include the assays	assays	confusion, drowsiness,
	disclosed in: Loweth, AC, et	AC, et	nonketotic hyperglycemic-
	al., FEBS Lett, 400(3):285-8	285-8	hyperosmolar coma,
	(1997); Saini, KS, et al.,	l.,	cardiovascular disease (e.g.,
	Biochem Mol Biol Int,		heart disease, atherosclerosis,
	39(6):1229-36 (1996);		microvascular disease,
	Krautheim, A., et al., B	3r J	hypertension, stroke, and other
	Pharmacol, 129(4):687-94	7-94	diseases and disorders as
	(2000); Chandra J, et al.,	II.,	described in the
	Diabetes, 50 Suppl 1:S44-7	44-7	"Cardiovascular Disorders"
	(2001); Suk K, et al., J		section below), dyslipidemia,
	Immunol, 166(7):4481-9	6-	endocrine disorders (as
•	(2001); Tejedo J, et al., FEBS	, FEBS	described in the "Endocrine
	Lett, 459(2):238-43 (1999);	999);	Disorders" section below),
	Zhang, S., et al., FEBS Lett,	Lett,	neuropathy, vision impairment
	455(3):315-20 (1999); Lee et	Lee et	(e.g., diabetic retinopathy and
	al., FEBS Lett 485(2-3): 122-): 122-	blindness), ulcers and impaired
	126 (2000); Nor et al., J Vasc	J Vasc	wound healing, and infection
	Res 37(3): 209-218 (2000);	000);	(e.g., infectious diseases and
	and Karsan and Harlan, J	1, J	disorders as described in the
	Atheroscler Thromb 3(2): 75-	(2): 75-	"Infectious Diseases" section
	80 (1996); the contents of each		below, especially of the

			of which are herein	urinary tract and skin), carpal
			incorporated by reference in its	tunnel syndrome and
			entirety. Pancreatic cells that	Dupuytren's contracture).
			may be used according to these	An additional highly preferred
			assays are publicly available	indication is obesity and/or
			(e.g., through the ATCC)	complications associated with
			and/or may be routinely	obesity. Additional highly
			generated. Exemplary	preferred indications include
 -		-	pancreatic cells that may be	weight loss or alternatively,
			used according to these assays	weight gain. Aditional
			include RIN-m. RIN-m is a	highly preferred indications are
		<u>.</u>	rat adherent pancreatic beta	complications associated with
			cell insulinoma cell line	insulin resistance.
			derived from a radiation	
•			induced transplantable rat islet	
			cell tumor. The cells produce	
			and secrete islet polypeptide	
			hormones, and produce insulin,	
			somatostatin, and possibly	
			glucagon. ATTC: #CRL-2057	
			Chick et al. Proc. Natl. Acad.	
			Sci. 1977 74:628; AF et al.	
		٠	Proc. Natl. Acad. Sci. 1980	
			77:3519.	
 HOSFD58	692	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
		Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
		Signaling Pathway.	transduction that regulate cell	described below under
			proliferation, activation, or	"Hyperproliferative
			apoptosis are well known in	Disorders"), blood disorders
			the art and may be used or	(e.g., as described below under
			routinely modified to assess	"Immune Activity",

	the ability of polypeptides of	"Cardiovascular Disorders",
	the invention (including	and/or "Blood-Related
	antibodies and agonists or	Disorders"), and infection
	antagonists of the invention) to	(e.g., an infectious disease as
-	promote or inhibit immune cell	described below under
-	(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
	activation, and apoptosis.	preferred indications include
	Exemplary assays for JNK and	autoimmune diseases (e.g.,
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,
	are herein incorporated by	lung, colon, pancreatic,
	reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver, and urinary cancer. Other
	according to these assays are	preferred indications include

 			publicly available (e.g.,	benign dysproliferative
			through the ATCC).	disorders and pre-neoplastic
			Exemplary mouse T cells that	conditions, such as, for
			may be used according to these	example, hyperplasia,
			assays include the CTLL cell	metaplasia, and/or dysplasia.
			line, which is an IL-2	Preferred indications include
 			dependent suspension-culture	arthritis, asthma, AIDS,
			cell line with cytotoxic	allergy, anemia, pancytopenia,
			activity.	leukopenia, thrombocytopenia,
				Hodgkin"s disease, acute
 				lymphocytic anemia (ALL),
		-		plasmacytomas, multiple
				myeloma, Burkitt"s lymphoma,
				granulomatous disease,
				inflammatory bowel disease,
				sepsis, psoriasis, suppression
				of immune reactions to
				transplanted organs and
				tissues, endocarditis,
				meningitis, and Lyme Disease.
HPDDC77	1770	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
		Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
		Signaling Pathway.	transduction that regulate cell	described below under
			proliferation, activation, or	"Hyperproliferative
			apoptosis are well known in	Disorders"), blood disorders
			the art and may be used or	(e.g., as described below under
			routinely modified to assess	"Immune Activity",
			the ability of polypeptides of	"Cardiovascular Disorders",
			the invention (including	and/or "Blood-Related
			antibodies and agonists or	Disorders"), and infection
			antagonists of the invention) to	(e.g., an infectious disease as

	I nromote or inhihit immine cell	described below under
	(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
	activation, and apoptosis.	preferred indications include
	Exemplary assays for JNK and	autoimmune diseases (e.g.,
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
-	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
-	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,
	are herein incorporated by	lung, colon, pancreatic,
	reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver, and urinary cancer. Other
	according to these assays are	preferred indications include
	publicly available (e.g.,	benign dysproliferative
	through the ATCC).	disorders and pre-neoplastic
	Exemplary mouse T cells that	conditions, such as, for
	may be used according to these	example, hyperplasia,

· · · · · · · · · · · · · · · · · · ·		——	
metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.			A highly preferred indication is diabetes mellitus. Additional highly preferred indications include complications associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other
assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.			Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the
	IL-2 in Human T cells	Caspase (+paclitaxel) in SW480	Regulation of transcription via DMEF1 response element in adipocytes and preadipocytes
·	770	770	177
	HPDDC77	HPDDC77	HPEAD79

		DMCET accepted clomont in a	diseases and disorders as
		DIMER I response element in a	diseases and disorders as
		reporter construct (such as that	described in the "Kenal
		containing the GLUT4	Disorders" section below),
		promoter) and to regulate	diabetic neuropathy, nerve
		insulin production. The	disease and nerve damage
		DMEF1 response element is	(e.g., due to diabetic
		present in the GLUT4	neuropathy), blood vessel
		promoter and binds to MEF2	blockage, heart disease, stroke,
		transcription factor and another	impotence (e.g., due to diabetic
		transcription factor that is	neuropathy or blood vessel
		required for insulin regulation	blockage), seizures, mental
		of Glut4 expression in skeletal	confusion, drowsiness,
		muscle. GLUT4 is the primary	nonketotic hyperglycemic-
		insulin-responsive glucose	hyperosmolar coma,
		transporter in fat and muscle	cardiovascular disease (e.g.,
		tissue. Exemplary assays that	heart disease, atherosclerosis,
		may be used or routinely	microvascular disease,
		modified to test for DMEF1	hypertension, stroke, and other
		response element activity (in	diseases and disorders as
		adipocytes and pre-adipocytes)	described in the
		by polypeptides of the	"Cardiovascular Disorders"
		invention (including antibodies	section below), dyslipidemia,
		and agonists or antagonists of	endocrine disorders (as
		the invention) include assays	described in the "Endocrine
		disclosed inThai, M.V., et al., J	Disorders" section below),
	-	Biol Chem, 273(23):14285-92	neuropathy, vision impairment
		(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
-		Chem, 275(21):16323-8	blindness), ulcers and impaired
		(2000); Liu, M.L., et al., J Biol	wound healing, and infection
		Chem, 269(45):28514-21	(e.g., infectious diseases and
		(1994); "Identification of a 30-	disorders as described in the

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"Infectious Diseases" section below, especially of the urinary tract and skin). An additional highly preferred indication is obesity and/or		preferred indications include weight loss or alternatively, weight gain. Additional highly	preferred indications are complications associated with	insulin resistance.															
base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice". J Biol Chem.	2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10	(1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the	contents of each of which is herein incorporated by	reference in its entirety. Adinocytes and pre-adinocytes	that may be used according to	these assays are publicly available (e.g., through the	ATCC) and/or may be	routinely generated.	Exemplary cells that may be used according to these assays	include the mouse 3T3-L1 cell	line which is an adherent	mouse preadipocyte cell line.	Mouse 3T3-L1 cells are a	continuous substrain of 3T3	fibroblasts developed through	clonal isolation. These cells	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation

				culture conditions.	
	HPFCL43	772	SEAP in ATP-3T3- L1		
	HPFCL43	772	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
_			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
_				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
				Proc Natl Acad Sci USA	suppressing a T cell-mediated
				85:6342-6346 (1988); and	immune response. Additional

	Blac 12(2		highly preferred indications include inflammation and
	cont	content of each of which are herein incorporated by	inflammatory disorders, and treating joint damage in
	refe	reference in its entirety. T	patients with rheumatoid
	cells	cells that may be used	arthritis. An additional highly
	acc	according to these assays are	preferred indication is sepsis.
	qnd	publicly available (e.g.,	Highly preferred indications
	thro	through the ATCC).	include neoplastic diseases
_	Exe	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may	may be used according to these	and/or as described below
	assa	assays include the CTLL cell	under "Hyperproliferative
	line	line, which is an IL-2	Disorders"). Additionally,
	deb deb	dependent suspension culture	highly preferred indications
		of T cells with cytotoxic	include neoplasms and
_	acti	activity.	cancers, such as, for example,
			leukemia, lymphoma,
			melanoma, glioma (e.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
-			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,

leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease
		Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including
	Caspase (+camptothecin) in SW480	Regulation of viability and proliferation of pancreatic beta cells.
	772	773
	HPFCL43	HPIBO15

		antibodies and agonists or	(e.g., renal failure,
		antagonists of the invention) to	nephropathy and/or other
		regulate viability and	diseases and disorders as
		proliferation of pancreatic beta	described in the "Renal
		cells. For example, the Cell	Disorders" section below),
		Titer-Glo luminescent cell	diabetic neuropathy, nerve
		viability assay measures the	disease and nerve damage
		number of viable cells in	(e.g., due to diabetic
		culture based on quantitation	neuropathy), blood vessel
		of the ATP present which	blockage, heart disease, stroke,
		signals the presence of	impotence (e.g., due to diabetic
		metabolically active cells.	neuropathy or blood vessel
		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
		test regulation of viability and	nonketotic hyperglycemic-
		proliferation of pancreatic beta	hyperosmolar coma,
		cells by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
-		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Friedrichsen BN,	diseases and disorders as
		et al., Mol Endocrinol,	described in the
		15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
		MA, et al., Endocrinology,	section below), dyslipidemia,
		139(4):1494-9 (1998); Hugl	endocrine disorders (as
		SR, et al., J Biol Chem 1998	described in the "Endocrine
		Jul 10;273(28):17771-9	Disorders" section below),
		(1998), the contents of each of	neuropathy, vision impairment
		which is herein incorporated	(e.g., diabetic retinopathy and
		by reference in its entirety.	blindness), ulcers and impaired
		Pancreatic cells that may be	wound healing, and infection

(e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include
used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semiadherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases.
	Production of IL-6
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	HPIBO15

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blood disorders (e.g., as described below under	"Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	disorders. Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,
Assays for immunomodulatory and differentiation factor	proteins produced by a large variety of cells where the	expression level is strongly	regulated by cytokines, growth	factors, and hormones are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and
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		36	agonists or antagonists of the	leukemia, lymphoma,
		9.5	nvention) include assays	melanoma, and/or as described
 		-	disclosed in Miraglia et al., J	below under
		Bi	Biomolecular Screening 4:193-	"Hyperproliferative
		20	204(1999); Rowland et al.,	Disorders"). Highly preferred
		<u> </u>	"Lymphocytes: a practical	indications include neoplasms
		ap	approach" Chapter 6:138-160	and cancers, such as, myeloma,
		(2)	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	`		Immunol 158:2919-2925	lymphoma, melanoma, and
		(1)	(1997), the contents of each of	prostate, breast, lung, colon,
			which are herein incorporated	pancreatic, esophageal,
		- ps	by reference in its entirety.	stomach, brain, liver and
 		H	Human dendritic cells that may	urinary cancer. Other preferred
		<u></u>	be used according to these	indications include benign
		as	assays may be isolated using	dysproliferative disorders and
		Ţ.	techniques disclosed herein or	pre-neoplastic conditions, such
		to Ot	otherwise known in the art.	as, for example, hyperplasia,
		H	Human dendritic cells are	metaplasia, and/or dysplasia.
		<u>a</u>	antigen presenting cells in	Preferred indications include
		ns	suspension culture, which,	anemia, pancytopenia,
		M	when activated by antigen	leukopenia, thrombocytopenia,
		a	and/or cytokines, initiate and	Hodgkin's disease, acute
		'n	upregulate T cell proliferation	lymphocytic anemia (ALL),
		ar	and functional activities.	multiple myeloma, Burkitt's
				lymphoma, arthritis, AIDS,
				granulomatous disease,
				inflammatory bowel disease,
				sepsis, neutropenia,
-				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted

					organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious
	HPIBO15	773	Glucose Production in H4IIE		
	HPICB53	774	Endothelial Cell Apoptosis	Caspase Apoptosis. Assays for caspase apoptosis are well	A highly preferred embodiment of the invention
				known in the art and may be used or routinely modified to	includes a method for stimulating endothelial cell
•				assess the ability of polypeptides of the invention	growth. An alternative highly preferred embodiment of the
				(including antibodies and	invention includes a method
				agonists or antagonists of the invention) to promote caspase	for innibiting endothelial cell growth. A highly preferred
				protease-mediated apoptosis.	embodiment of the invention
				induction of apoptosis in endothelial cells supporting the	includes a method for stimulating endothelial cell
				vasculature of tumors is	proliferation. An alternative
				associated with tumor	highly preferred embodiment
				regression due to loss of fumor blood supply. Exemplary	of the invention includes a method for inhibiting
				assays for caspase apoptosis	endothelial cell proliferation.
				that may be used or routinely	A highly preferred
				modified to test capase	embodiment of the invention
				apoptosis activity of	includes a method for

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ig apopt	al cells.	e highly	ent of th	methoc	(e.g., de	of endo	preferre	ent of th	a method	ng angio	e highly	ent of th	a methoc	; angiog	eferred e	ention in	or reduci	hy. An	eferred e	ention in	or induci	hy.	indicati	c disease	below 1	oliferati	;"), and	vascula	
stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis.	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	•
noiti		fthe	says	EBS	2000);	(3):	san)();	/hich	ý		y be	ssays	ë;	rces).	ells	ing to	ine		ample	h line	/olved	, but			ne,	sation.	
polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Lee et al., FEBS	Lett 485(2-3): 122-126 (2000);	Nor et al., J Vasc Res 37(3):	209-218 (2000); and Karsan	and Harlan, J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	al cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	0,	ascular	permeability, vascular tone,	l extrava	
tides of	ng antib	s or anta	on) inclu	ed in Lee	5(2-3): 1	ıl., J Vas	8 (2000);	rlan, J A	3(2): 7:	tents of e	in incor	reference in its entirety.	elial cell	cording	licly ava	comme	lary endo	y be use	ssays inc	aortic endothelial cells), which	thelial co	essels ar	tions that	are not limited to,	angiogenesis, vascular	bility, va	and immune cell extravasation.	
polypep	(includi	agonists	inventic	disclose	Lett 48:	Nor et a	209-218	and Han	Thromb	the cont	are here	reference	Endothe	used ac	are pub	through	Exempl	that ma	these as	aortic e	(bAEC)	opua Jo	blood v	in funct	are not	angioge	permea	and im	
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			aortic stenosis,	
			cardiomyopathy, valvular	thy, valvular
			regurgitation,	regurgitation, left ventricular
			dysfunction,	dysfunction, atherosclerosis
		-	and atheroscl	and atherosclerotic vascular
			disease, diabe	disease, diabetic nephropathy,
			intracardiac s	intracardiac shunt, cardiac
			hypertrophy, myocardial	myocardial
		_	infarction, chronic	ronic
			hemodynamic	hemodynamic overload, and/or
			as described below under	below under
			"Cardiovascu	"Cardiovascular Disorders").
			Highly prefer	Highly preferred indications
			include cardiovascular,	iovascular,
-			endothelial ar	endothelial and/or angiogenic
			disorders (e.g., systemic	., systemic
	_		disorders that	disorders that affect vessels
			such as diabe	such as diabetes mellitus, as
			well as diseas	well as diseases of the vessels
			themselves, such as of the	uch as of the
			arteries, capillaries, veins	laries, veins
			and/or lymph	and/or lymphatics). Highly
			preferred are	preferred are indications that
			stimulate ang	stimulate angiogenesis and/or
-			cardiovascula	cardiovascularization. Highly
			preferred are	preferred are indications that
			inhibit angiog	inhibit angiogenesis and/or
			cardiovascularization.	ırization.
			Highly prefer	Highly preferred indications
			include antiar	include antiangiogenic activity
			to troot of the	,

leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides Revnaud"s
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			disease and Reynaud"s
		-	about the monomous and a
		_	pnenomenom, aneurysms,
		-	restenosis; venous and
	 		lymphatic disorders such as
			thrombophlebitis,
			lymphangitis, and
	 		lymphedema; and other
			vascular disorders such as
			peripheral vascular disease,
			and cancer. Highly
	 		preferred indications also
			include trauma such as
			wounds, burns, and injured
			tissue (e.g., vascular injury
			such as, injury resulting from
			balloon angioplasty, and
			atheroschlerotic lesions),
			implant fixation, scarring,
	 		ischemia reperfusion injury,
_	 		rheumatoid arthritis,
			cerebrovascular disease, renal
			diseases such as acute renal
	 		failure, and osteoporosis.
			Additional highly preferred
•			indications include stroke,
			graft rejection, diabetic or
			other retinopathies, thrombotic
	 		and coagulative disorders,
			vascularitis, lymph
			angiogenesis, sexual disorders,
			age-related macular

degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,	inflammatory bowel disease	and Crohn's disease), and pain	management.	A highly preferred
																														Assays for measuring secretion
						-								-						-					-					Stimulation of
					_								•																	775
						_																	_							HPJBI33
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	insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
	from pancreatic	the art and may be used or	An additional highly preferred
	beta cells.	routinely modified to assess	indication is a complication
		the ability of polypeptides of	associated with diabetes (e.g.,
		the invention (including	diabetic retinopathy, diabetic
		antibodies and agonists or	nephropathy, kidney disease
		antagonists of the invention) to	(e.g., renal failure,
		stimulate insulin secretion.	nephropathy and/or other
•		For example, insulin secretion	diseases and disorders as
		is measured by FMAT using	described in the "Renal
		anti-rat insulin antibodies.	Disorders" section below),
		Insulin secretion from	diabetic neuropathy, nerve
		pancreatic beta cells is	disease and nerve damage
	-	upregulated by glucose and	(e.g., due to diabetic
		also by certain	neuropathy), blood vessel
		proteins/peptides, and	blockage, heart disease, stroke,
		disregulation is a key	impotence (e.g., due to diabetic
		component in diabetes.	neuropathy or blood vessel
		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
		test for stimulation of insulin	nonketotic hyperglycemic-
		secretion (from pancreatic	hyperosmolar coma,
		cells) by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Ahren, B., et al.,	diseases and disorders as
		Am J Physiol, 277(4 Pt	described in the
	_	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
		al., Endocrinology,	section below), dyslipidemia,
		138(9):3735-40 (1997); Kim,	endocrine disorders (as

				K.H., et al., FEBS Lett.	described in the "Endocrine
				7707.077 0 (1006)	
-				(2)/(2):23/-9 (1993); and,	Disorders" section below),
				Miraglia S et. al., Journal of	neuropathy, vision impairment
				Biomolecular Screening,	(e.g., diabetic retinopathy and
		7.1.1		4:193-204 (1999), the contents	blindness), ulcers and impaired
				of each of which is herein	wound healing, and infection
		,		incorporated by reference in its	(e.g., infectious diseases and
				entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
				assays are publicly available	below, especially of the
		-		(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
				pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
		,		130:167.	
	HPJBI33	775	SEAP in SW480		
	HPJBK12	922	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred

	routinely modified to assess	indication is a complication
	the ability of polypeptides of	associated with diabetes (e.g.,
	the invention (including	diabetic retinopathy, diabetic
	antibodies and agonists or	nephropathy, kidney disease
	antagonists of the invention) to	
	stimulate insulin secretion.	nephropathy and/or other
	For example, insulin secretion	diseases and disorders as
	is measured by FMAT using	described in the "Renal
	anti-rat insulin antibodies.	Disorders" section below),
	Insulin secretion from	diabetic neuropathy, nerve
	pancreatic beta cells is	disease and nerve damage
	upregulated by glucose and	(e.g., due to diabetic
	also by certain	neuropathy), blood vessel
	proteins/peptides, and	blockage, heart disease, stroke,
	disregulation is a key	impotence (e.g., due to diabetic
	component in diabetes.	neuropathy or blood vessel
	Exemplary assays that may be	blockage), seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Shimizu, H., et	diseases and disorders as
-	al., Endocr J, 47(3):261-9	
	(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
	Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
	17 (1999); Filipsson, K., et al.,	endocrine disorders (as
	Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
	(1998); Olson, L.K., et al., J	Disorders" section below)

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somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551: Santerre et al. Proc.
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glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL- 1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551: Santerre et al. Proc.
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stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219:
stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551: Santerre et al. Proc.
stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551: Santerre et al. Proc.
stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551: Santerre et al. Proc.
stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219:
cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551: Santerre et al. Proc.
cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551: Santerre et al. Proc.
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glucocorticold receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219:
glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219:
glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551: Santerre et al. Proc.
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somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL- 1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551: Santerre et al. Proc.
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			4339-4343, 1981.	
 HPJBK12	922	Regulation of	Caspase Apoptosis. Assays for	Preferred embodiments of the
		apoptosis of	caspase apoptosis are well	invention include using
		immune cells (such	known in the art and may be	polypeptides of the invention
		as mast cells).	used or routinely modified to	(or antibodies, agonists, or
			assess the ability of	antagonists thereof) in
			polypeptides of the invention	detection, diagnosis,
			(including antibodies and	prevention, and/or treatment of
			agonists or antagonists of the	asthma, allergy,
			invention) to regulate caspase	hypersensitivity and
			protease-mediated apoptosis in	inflammation.
			immune cells (such as, for	
			example, in mast cells). Mast	
			cells are found in connective	
			and mucosal tissues throughout	
			the body, and their activation	
			via immunoglobulin E -	
			antigen, promoted by T helper	
			cell type 2 cytokines, is an	
			important component of	
			allergic disease. Dysregulation	
			of mast cell apoptosis may	
			play a role in allergic disease	
			and mast cell tumor survival.	
			Exemplary assays for caspase	
		-	apoptosis that may be used or	
			routinely modified to test	
			capase apoptosis activity	
			induced by polypeptides of the	
-			invention (including antibodies	
			and agonists or antagonists of	

HPJBK12	the invention) include the assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	Endothelial Cell kinase assay. JNK and p38 A highly preferred embodinent of the invention p38 or JNK transduction that regulate cell includes a method for signaling Pathway. proliferation, activation, or growth. An alternative highly the art and may be used or preferred embodiment of the
HPJBK12		

the abij	the ability of polypeptides of	for inhibiting endothelial cell
the inv		growth. A highly preferred
antibod	antibodies and agonists or	<u> </u>
antagor	antagonists of the invention) to	includes a method for
promot	promote or inhibit cell	stimulating endothelial cell
prolifer	proliferation, activation, and	proliferation. An alternative
apoptos	apoptosis. Exemplary assays	highly preferred embodiment
for JNK	for JNK and p38 kinase	of the invention includes a
activity	activity that may be used or	method for inhibiting
routine	routinely modified to test JNK	endothelial cell proliferation.
and p38	and p38 kinase-induced	A highly preferred
activity	activity of polypeptides of the	embodiment of the invention
inventi	invention (including antibodies	includes a method for
and ago	and agonists or antagonists of	stimulating apoptosis of
the inve	the invention) include the	endothelial cells. An
assays	assays disclosed in Forrer et	alternative highly preferred
al., Bio	al., Biol Chem 379(8-9):1101-	embodiment of the invention
1110(1	Exp	includes a method for
Cell Re	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
(1999);	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
Soc Syl	Soc Symp 64:29-48 (1999);	A highly preferred
Chang		embodiment of the invention
410(68)		includes a method for
Cobb N		stimulating (e.g., increasing)
Biol 71	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
the con	ich	alternative highly preferred
are here	are herein incorporated by	embodiment of the invention
referen		includes a method for
Endoth	Endothelial cells that may be	inhibiting (e.g., decreasing) the
used ac	lys	activation of and/or
are pub	are publicly available (e.g.,	inactivating endothelial cells.

		through the ATCC).	A highly preferred
		Exemplary endothelial cells	embodiment of the invention
		that may be used according to	includes a method for
		these assays include human	stimulating angiogenisis. An
		umbilical vein endothelial cells	alternative highly preferred
		(HUVEC), which are	embodiment of the invention
	-	endothelial cells which line	includes a method for
		venous blood vessels, and are	inhibiting angiogenesis. A
		involved in functions that	highly preferred embodiment
		include, but are not limited to,	of the invention includes a
		angiogenesis, vascular	method for reducing cardiac
_		permeability, vascular tone,	hypertrophy. An alternative
		and immune cell extravasation.	highly preferred embodiment
-			of the invention includes a
			method for inducing cardiac
	7		hypertrophy. Highly
			preferred indications include
			neoplastic diseases (e.g., as
			described below under
			"Hyperproliferative
-			Disorders"), and disorders of
			the cardiovascular system
			(e.g., heart disease, congestive
			heart failure, hypertension,
			aortic stenosis,
			cardiomyopathy, valvular
			regurgitation, left ventricular
			dysfunction, atherosclerosis
			and atherosclerotic vascular
			disease, diabetic nephropathy,
			intracardiac shunt, cardiac

hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	hemangioma (capillary and	cavernous), glomus fumors
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telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud's	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other
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vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and
																			-											

				vascular disease
				Preferred indications include
				The 11 To a marcanons monde
				blood disorders (e.g., as
-				described below under
				"Immune Activity", "Blood-
				Related Disorders", and/or
				"Cardiovascular Disorders").
				Preferred indications include
				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
				described below). Additional
				preferred indications include
				inflammation and
				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HPMDK28	777	Stimulation of	Assays for measuring calcium	A highly preferred
		Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
		pancreatic beta	and may be used or routinely	An additional highly preferred
		cells.	modified to assess the ability	indication is a complication
			of polypeptides of the	associated with diabetes (e.g.,
			invention (including antibodies	diabetic retinopathy, diabetic
			and agonists or antagonists of	nephropathy, kidney disease
			the invention) to mobilize	(e.g., renal failure,

nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),	diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel	blockage), heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental	confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g.,	heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the	"Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below),	neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection
calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low	concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause	an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell	functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the	invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Satin LS, et al., Endocrinology, 136(10):4589-	601 (1995); Mogami H, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al.,	Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is herein incorporated by

			Pancreatic cells that may be used according to these assays	disorders as described in the
			are publicly available (e.g.,	below, especially of the
			through the ATCC) and/or	urinary tract and skin), carpal
			may be routinely generated.	tunnel syndrome and
	_		Exemplary pancreatic cells that	Dupuytren's contracture).
			may be used according to these	An additional highly preferred
			assays include HITT15 Cells.	indication is obesity and/or
			HITT15 are an adherent	complications associated with
			epithelial cell line established	obesity. Additional highly
			from Syrian hamster islet cells	preferred indications include
			transformed with SV40. These	weight loss or alternatively,
			cells express glucagon,	weight gain. Aditional
			somatostatin, and	highly preferred indications are
			glucocorticoid receptors. The	complications associated with
			cells secrete insulin, which is	insulin resistance.
			stimulated by glucose and	
			glucagon and suppressed by	
			somatostatin or	
			glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
TINATOR			4339-4343, 1981.	
HPMDK28	///	SEAP in Jurkat/IL4 promoter (antiCD3		
		co-stim)		
HPMFP40	778	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,

immune cells (such
as T-cells).

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preferred indication is sepsis. Highly preferred indications	include neoplastic diseases (e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous
according to these assays are publicly available (e.g.,	through the AICC). Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of I cells with cytotoxic	activity.																					
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					disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease")
臣	HPRAL78	779	Regulation of transcription via DMEF1 response element in adipocytes and preadipocytes	Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The DMEF1 response element is	A highly preferred indication is diabetes mellitus. Additional highly preferred indications include complications associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic

			present in the GLUT4	neuropathy), blood vessel
			promoter and binds to MEF2	blockage, heart disease, stroke,
			transcription factor and another	impotence (e.g., due to diabetic
			transcription factor that is	neuropathy or blood vessel
			required for insulin regulation	blockage), seizures, mental
			of Glut4 expression in skeletal	confusion, drowsiness,
			muscle. GLUT4 is the primary	nonketotic hyperglycemic-
			insulin-responsive glucose	hyperosmolar coma,
			transporter in fat and muscle	cardiovascular disease (e.g.,
			tissue. Exemplary assays that	heart disease, atherosclerosis,
			may be used or routinely	microvascular disease,
			modified to test for DMEF1	hypertension, stroke, and other
			response element activity (in	diseases and disorders as
			adipocytes and pre-adipocytes)	described in the
-			by polypeptides of the	"Cardiovascular Disorders"
-			invention (including antibodies	section below), dyslipidemia,
	_		and agonists or antagonists of	endocrine disorders (as
			the invention) include assays	described in the "Endocrine
			disclosed in Thai, M.V., et al., J	Disorders" section below),
		3.0	Biol Chem, 273(23):14285-92	neuropathy, vision impairment
			(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
			Chem, 275(21):16323-8	blindness), ulcers and impaired
			(2000); Liu, M.L., et al., J Biol	wound healing, and infection
			Chem, 269(45):28514-21	(e.g., infectious diseases and
			(1994); "Identification of a 30-	disorders as described in the
	-		base pair regulatory element	"Infectious Diseases" section
	•		and novel DNA binding	below, especially of the
			protein that regulates the	urinary tract and skin). An
			human GLUT4 promoter in	additional highly preferred
			transgenic mice", J Biol Chem.	indication is obesity and/or
			2000 Aug 4;275(31):23666-73;	complications associated with

Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line. Which is an adherent mouse preadipocyte cell line. Mouse 5T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. HPRAL78 779 1L-2 in Human T- appropriate differentiation culture conditions. HPRAL78 779 1L-2 in Human T- appropriate differentiation culture conditions. HPRAL78 779 8EAP in OB-33 HPRAL78 780 8EAP in HB/CRE	et al., preferred indicational highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. ocytes ing to y be assays 1 cell t t line. a 3T3 rough cells to under				
779	Berger, et al., Gene 66: (1988); and, Cullen, B., Methods in Enzymol. 216:362–368 (1992), the contents of each of which herein incorporated by reference in its entirety. Adipocytes and pre-adipthat may be used accord these assays are publicly available (e.g., through ATCC) and/or may be routinely generated. Exemplary cells that maused according to these include the mouse 3T3-line which is an adheren mouse preadipocyte cell Mouse 3T3-L1 cells are continuous substrain of fibroblasts developed the clonal isolation. These quadipose-like conversion appropriate differentiatiic culture conditions.				
		IL-2 in Human T-cell 293T	SEAP in OE-33	VEGF in SW480	SEAP in HIB/CRE
HPRAL78 HPRAL78 HPRAL78 HPRAL78		779	779	779	780
		HPRAL78	HPRAL78	HPRAL78	HPRBC80

	HPRBC80	780	Activation of	This reporter assay measures	Highly preferred indications
-			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred
				through the GATA3 response	indications include neoplastic
				element that may be used or	diseases (e.g., leukemia,
				routinely modified to test	lymphoma, melanoma,
				GATA3-response element	prostate, breast, lung, colon,
				activity of polypeptides of the	pancreatic, esophageal,
				invention (including antibodies	stomach, brain, liver, and
				and agonists or antagonists of	urinary tract cancers and/or as
				the invention) include assays	described below under

Γ																														_	-
	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, and Lyme Disease.						
	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	that may be used according to	these assays include the HMC-	1 cell line, which is an	immature human mast cell line	established from the peripheral	blood of a patient with mast	cell leukemia, and exhibits	many characteristics of	
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	_																														_

					_		_																					
Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred	indications include infection	(e.g., an infectious disease as	described below under	"Infectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under
This reporter assay measures activation of the NFAT signaling pathway in HMC-1	human mast cell line.	Activation of NFAT in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the Nuclear Factor of	Activated T cells (NFAT)	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and
Activation of transcription through NFAT	response element in	immune cells (such	as mast cells).												•													
780					-																							
HPRBC80																								_				

	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia
-	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,
	which are herein incorporated	sepsis, neutropenia,
	by reference in its entirety.	neutrophilia, psoriasis,
	Mast cells that may be used	suppression of immune
	according to these assays are	reactions to transplanted
	publicly available (e.g.,	organs and tissues, hemophilia,
	through the ATCC).	hypercoagulation, diabetes
	Exemplary human mast cells	mellitus, endocarditis,
	that may be used according to	meningitis, and Lyme Disease.
	these assays include the HMC-	
	1 cell line, which is an	
	immature human mast cell line	
	established from the peripheral	
	blood of a patient with mast	
	cell leukemia, and exhibits	

				many characteristics of	
				immature mast cells.	
	HPRBC80	780	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
			cells).	modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
-				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
	0.00			modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
-				transcription through the	cell-mediated immune
	-		,	NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
			-	polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an
				agonists or antagonists of the	infectious disease as described
				invention) include assays	below under "Infectious
				disclosed in Berger et al., Gene	Disease"). Preferred
				66:1-10 (1998); Cullen and	indications include neoplastic
				Malm, Methods in Enzymol	diseases (e.g., leukemia,
				216:362-368 (1992); Henthorn	lymphoma, and/or as described

at al Droc Natl Acad Sci 11SA	helow under
or (24) (100)	.' J: 1: 0: 1
85:6342-6346 (1988);	"Hyperproliterative
Aramburu et al., J Exp Med	Disorders"). Preferred
182(3):801-810 (1995); De	indications include neoplasms
Boer et al., Int J Biochem Cell	and cancers, such as, for
Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
Fraser et al., Eur J Immunol	and prostate, breast, lung,
29(3):838-844 (1999); and	colon, pancreatic, esophageal,
Yeseen et al., J Biol Chem	stomach, brain, liver and
268(19):14285-14293 (1993),	urinary cancer. Other preferred
the contents of each of which	indications include benign
are herein incorporated by	dysproliferative disorders and
reference in its entirety. NK	pre-neoplastic conditions, such
cells that may be used	as, for example, hyperplasia,
according to these assays are	metaplasia, and/or dysplasia.
publicly available (e.g.,	Preferred indications also
through the ATCC).	include anemia, pancytopenia,
Exemplary human NK cells	leukopenia, thrombocytopenia,
that may be used according to	Hodgkin's disease, acute
these assays include the NK-	lymphocytic anemia (ALL),
YT cell line, which is a human	plasmacytomas, multiple
natural killer cell line with	myeloma, Burkitt's lymphoma,
cytolytic and cytotoxic	arthritis, AIDS, granulomatous
activity.	disease, inflammatory bowel
	disease, sepsis, neutropenia,
	neutrophilia, psoriasis,
	suppression of immune
	reactions to transplanted
	organs and tissues,
	hemophilia, hypercoagulation,
	diabetes mellitus, endocarditis,

					meningitis, Lyme Disease, asthma and allergy
	HPRBC80	780	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
_				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
-				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn's disease, multiple
				invention (including antibodies	sclerosis and/or as described
	•			and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and
_				Malm, Methods in Enzymol	suppressing a T cell-mediated
_	-			216:362-368 (1992); Henthorn	immune response. Additional
	~			et al., Proc Natl Acad Sci USA	highly preferred indications

		85:6342-6346 (1988); Benson	include inflammation and
	-	et al., J Immunol 153(9):3862-	inflammatory disorders, and
		3873 (1994); and Black et al.,	treating joint damage in
		Virus Genes 12(2):105-117	patients with rheumatoid
		(1997), the content of each of	arthritis. An additional highly
		which are herein incorporated	preferred indication is sepsis.
		by reference in its entirety. T	Highly preferred indications
		cells that may be used	include neoplastic diseases
		according to these assays are	(e.g., leukemia, lymphoma,
		publicly available (e.g.,	and/or as described below
		through the ATCC).	under "Hyperproliferative
		Exemplary T cells that may be	Disorders"). Additionally,
		used according to these assays	highly preferred indications
		include the NK-YT cell line,	include neoplasms and
		which is a human natural killer	cancers, such as, for example,
		cell line with cytolytic and	leukemia, lymphoma,
		cytotoxic activity.	melanoma, glioma (e.g.,
			malignant glioma), solid
_			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,

				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
-				disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
	-			organs and tissues, hemophilia,
				hypercoagulation, diabetes
				mellitus, endocarditis,
-				meningitis, Lyme Disease,
-				cardiac reperfusion injury, and
				asthma and allergy. An
 				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
 HPRBC80	780	Activation of	Assays for the activation of	Preferred indications
		transcription	transcription through the AP1	include neoplastic diseases
		through AP1	response element are well-	(e.g., as described below under
		response element in	known in the art and may be	"Hyperproliferative
		immune cells (such	used or routinely modified to	Disorders"), blood disorders
		as T-cells).	assess the ability of	(e.g., as described below under
			polypeptides of the invention	"Immune Activity",
			(including antibodies and	"Cardiovascular Disorders",
			agonists or antagonists of the	and/or "Blood-Related
			invention) to modulate growth	Disorders"), and infection
			and other cell functions.	(e.g., an infectious disease as

		Exemplary assays for	described below under
		transcription through the AP1	"Infectious Disease"). Highly
		response element that may be	preferred indications include
		used or routinely modified to	autoimmune diseases (e.g.,
		test AP1-response element	rheumatoid arthritis, systemic
		activity of polypeptides of the	lupus erythematosis, multiple
		invention (including antibodies	sclerosis and/or as described
		and agonists or antagonists of	below) and
		the invention) include assays	immunodeficiencies (e.g., as
		disclosed in Berger et al., Gene	described below). Additional
	-	66:1-10 (1988); Cullen and	highly preferred indications
		Malm, Methods in Enzymol	include inflammation and
		216:362-368 (1992); Henthorn	inflammatory disorders.
		et al., Proc Natl Acad Sci USA	Highly preferred indications
		85:6342-6346 (1988);	also include neoplastic
		Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
		272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
		18(9):4986-4993 (1998); and	"Hyperproliferative
		Fraser et al., Eur J Immunol	Disorders"). Highly preferred
-		29(3):838-844 (1999), the	indications include neoplasms
		contents of each of which are	and cancers, such as, leukemia,
		herein incorporated by	lymphoma, prostate, breast,
		reference in its entirety.	lung, colon, pancreatic,
		Human T cells that may be	esophageal, stomach, brain,
		used according to these assays	liver, and urinary cancer. Other
		are publicly available (e.g.,	preferred indications include
		through the ATCC).	benign dysproliferative
		Exemplary human T cells that	disorders and pre-neoplastic
		may be used according to these	conditions, such as, for
		assays include the SUPT cell	example, hyperplasia,

		-	line, which is an IL-2 and IL-4 responsive suspension-culture cell line.	metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis	Г
HPRBC80	780	Activation of transcription through NFAT response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T	T

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essing a	ne	I highly	s includ		lers. A	eferred	on (e.g.,	s descril	ious	rred	neoplasi	mia,	s descri			pa	neoplasi	, for	lympho	lung,	ophage	r and	r prefer	enign	rders ar	tions, su	erplasia	ysplasia	also
d suppr	d imm	ditiona	lication	n and	y disore	ghly pr	infection	sease as	"Infect	Preferred	nclude 1	., leuke	ind/or a		erative	Preferr	nclude 1	such as	kemia,	breast,	eatic, es	in, live	er. Othe	sclude b	ive diso	c condi	ole, hyp	nd/or d	ications
response, and suppressing a T	cell-mediated immune	response. Additional highly	preferred indications include	inflammation and	inflammatory disorders. An	additional highly preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious	Disease").	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also
resp	-les	resp	prefe	infla	infla	addi	indic	infec	belo		indic						indic	and c	exan	and p	color	stom	urina	indic	dysp	pre-n	as, fo	meta	Prefe
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ys for	ough th	elemer	routine	NFAT.	nt activi	the inve	odies an	gonists	de assa	ger et a	Cullen	in Enz	992); Ho	Acad S	1988); S	3iophys	000); D	hem Ce	36 (199	. J Imm	1999); a	3iol Ch	(4293 (ach of v	orated	ntirety.	pesn :	se assay	e (e.g.,
ary assa	otion th	esbouse	used or	d to test	elemei	ides of	ng antib	or anta	n) inclu	d in Ber	(1998);	fethods	-368 (19	oc Natl	-6346 (1	ochim E	1-18 (2)	J Biocl	221-123	al., Eur	8-844 (t al., J I	14285-1	nts of e	n incorp	in its e	may be	g to thes	availabl
Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Serfling	et al., Biochim Biophys Acta	1498(1):1-18 (2000); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,
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leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the
	Activation of transcription through NFKB response element in immune cells (such as T-cells).
	780
	HPRBC80

may be used or rountinely modified to test NFKB- midbuding antibodies and additional highly preferred indications include assays are publicly available (e.g., melanoma, rend cancers, such as 19(3):838-844 (1999), the contents of each of which are herein incorporated by referred indications include through the ATCC). Exemplary human T cells that may be used according to these assays are publicly available (e.g., melanoma, rend cancers, such as 19(3):838-844 (1999), the contents of each of which are publicly available (e.g., melanoma, rend cancers, such as 19(3):838-844 (1999), the contents of each of which are publicly available (e.g., melanoma, rend cancers, such as 19(3):838-844 (1999), the contents of each of which are publicly available (e.g., melanoma, and prostate, through the ATCC). Exemplary human T cells that may be used according to these assays are publicly available (e.g., melanoma, and prostate, through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell metaplasia, and/or dysplasia. Preferred indications also include amemia, pancytopenia,	Se T 2 2 2 3 2 1 1 1 1 1 2 2 3 3 1 1 1 1 1 1
NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	MFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplaty human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.

				Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted
HPTTG19	781	Endothelial Cell Apoptosis	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a

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endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative
assays for caspase apoptosis	that may be used or routinely	modified to test capase	apoptosis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Lee et al., FEBS	Lett 485(2-3): 122-126 (2000);	Nor et al., J Vasc Res 37(3):	209-218 (2000); and Karsan	and Harlan, J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular
	*							-																						

and immune cell extravasation. (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, elft ventricular dysfunction, atheroselerosis and atheroselerosis and atheroselerosis and atheroselerosis and atheroselerosis intracardiae shunt, cardiae hypertrophy, myocardial infarction, chronic hypertrophy, myocardiad infarction, chronic chronic hypertrophy, myocardiad infarction, chronic hypertrophy, myocardiad and/or as described below under "Cardiovasculata Disorders". Highly preferred indications indications and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovasculatization. Highly preferred are indications that inhibit angiogenesis and/or cardiovasculatization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.		permeability, vascular tone,	Disorders"), and disorders of
heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, anterosclerosis and atherosclerosis and atherosclerosis and atherosclerosis and atherosclerosis and atherosclerosis and atherosclerosis intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders (e.g., systemic disorders that affect vessels such as disbetes mellitus, as well as diseases of the vessels such as disbetes mellitus, as well as diseases of the exterice, such as of the arteries, cardiovasculariarion shat stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.		and immune cell extravasation.	the cardiovascular system
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regurgitation, left ventricular dysfunction, atheroselerosis and atheroselerosis and atheroselerotic vascular disease, diabetic nephropathy, intracardiae shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders (e.g., systemic disorders that affect vessels such as diseases of the atteries, capillaries, veins and/or lymphatics). Highly preferred are indications that simulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.	-		aortic stenosis,
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Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or inhibit angiogenesis and/or			"Cardiovascular Disorders").
include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or			Highly preferred indications
endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or inhibit angiogenesis and/or inhibit angiogenesis and/or			include cardiovascular,
disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or inhibit angiogenesis and/or inhibit angiogenesis and/or inhibit angiogenesis and/or			endothelial and/or angiogenic
disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or			disorders (e.g., systemic
such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or inhibit angiogenesis and/or			disorders that affect vessels
well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or inhibit angiogenesis and/or			such as diabetes mellitus, as
themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or			well as diseases of the vessels
arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or			themselves, such as of the
and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or			arteries, capillaries, veins
preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or			and/or lymphatics). Highly
stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or			preferred are indications that
cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or			stimulate angiogenesis and/or
preferred are indications that inhibit angiogenesis and/or			cardiovascularization. Highly
inhibit angiogenesis and/or		,	preferred are indications that
			inhibit angiogenesis and/or

cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neonlasms and cancer	such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma,	lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease.

such as, atherosclerosis, hypertension, coronary artery	disease, inflammatory	vascullines, reynand s disease and Reynaud's	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic
			-	<u>-</u>						·										-						-		
				_				_	•		- •																	
															-													

and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatomy disasses a a
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		-				-										-	_											_		

					inflammatory bowel disease and Crohn's disease), and pain management.
	HPZAB47	782	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
				antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as
				promote or inhibit immune cell	described below under
				(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
-				activation, and apoptosis.	preferred indications include
				Exemplary assays for JNK and	autoimmune diseases (e.g.,
				p38 kinase activity that may be	rheumatoid arthritis, systemic
				used or routinely modified to	lupus erythematosis, multiple
				test JNK and p38 kinase-	sclerosis and/or as described
				induced activity of	below) and
_				polypeptides of the invention	immunodeficiencies (e.g., as
				(including antibodies and	described below). Additional
				agonists or antagonists of the	highly preferred indications
				invention) include the assays	include inflammation and
,				disclosed in Forrer et al., Biol	inflammatory disorders.
				Chem 379(8-9):1101-1110	Highly preferred indications
	•			(1998); Gupta et al., Exp Cell	also include neoplastic
				Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
				Kyriakis JM, Biochem Soc	lymphoma, and/or as described

			Symp 64.79-48 (1999): Chang	helow under
			and Karin Nature	"Hymorum Jifomativo
			410(6824):37-40 (2001): and	11) perpronneranve Disorders") Highly preferred
			Cobb MH. Prog Biophys Mol	indications include neonlasms
			Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
			the contents of each of which	lymphoma, prostate, breast,
			are herein incorporated by	lung, colon, pancreatic,
			reference in its entirety. T	esophageal, stomach, brain,
			cells that may be used	liver, and urinary cancer. Other
			according to these assays are	preferred indications include
			publicly available (e.g.,	benign dysproliferative
			through the ATCC).	disorders and pre-neoplastic
			Exemplary mouse T cells that	conditions, such as, for
			may be used according to these	example, hyperplasia,
			assays include the CTLL cell	metaplasia, and/or dysplasia.
			line, which is an IL-2	Preferred indications include
			dependent suspension-culture	arthritis, asthma, AIDS,
			cell line with cytotoxic	allergy, anemia, pancytopenia,
			activity.	leukopenia, thrombocytopenia,
				Hodgkin"s disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				granulomatous disease,
				inflammatory bowel disease,
				sepsis, psoriasis, suppression
				of immune reactions to
				transplanted organs and
				tissues, endocarditis,
				meningitis, and Lyme Disease.
HPZAB47	782	CD152 in Human T		

			cells		
	HPZAB47	782	Activation of	Assays for the activation of	Preferred embodiments of the
			transcription	transcription through the	invention include using
_			through NFKB	NFKB response element are	polypeptides of the invention
			response element in	well-known in the art and may	(or antibodies, agonists, or
			neuronal cells (such	be used or routinely modified	antagonists thereof) in
			as SKNMC cells).	to assess the ability of	detection, diagnosis,
				polypeptides of the invention	prevention, and/or treatment of
				(including antibodies and	Neurological Diseases and
				agonists or antagonists of the	Disorders (e.g. Alzheimer"s
				invention) to regulate NFKB	Disease, Parkinson's Disease,
				transcription factors and	Brain Cancer, Seizures).
				modulate expression of	
				neuronal genes. Exemplary	
				assays for transcription	
				through the NFKB response	
				element that may be used or	
				routinely modified to test	
				NFKB-response element	
				activity of polypeptides of the	
				invention (including antibodies	
				and agonists or antagonists of	
				the invention) include assays	
				disclosed in: Gill JS, et al.,	
				Neurobiol Dis, 7(4):448-461	
				(2000); Tamatani M, et al., J	
				Biol Chem, 274(13):8531-	
				8538 (1999); Berger et al.,	
				Gene 66:1-10 (1998); Cullen	
				and Malm, Methods in	
				Enzymol 216:362-368 (1992);	

c Natl 342-6346 luez et al, 455-460 et al., J -810 et al., 9), the which are by may be lese assays le (e.g., I cells that ing to these KNMC	and p38 Preferred indications include neoplastic diseases (e.g., as described below under ution, or whyperproliferative nown in Disorders"), blood disorders (e.g., as described below under "Immune Activity", ptides of "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection vention) to (e.g., an infectious disease as
Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Neuronal cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary neuronal cells that may be used according to these assays include the SKNMC neuronal cell line.	Activation of T- Kinase assay. JNK and p38 Cell p38 or JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to
	HRAAB15 783

(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
 activation, and apoptosis.	preferred indications include
Exemplary assays for JNK and	autoimmune diseases (e.g.,
 p38 kinase activity that may be	rheumatoid arthritis, systemic
used or routinely modified to	lupus erythematosis, multiple
 test JNK and p38 kinase-	sclerosis and/or as described
 induced activity of	below) and
polypeptides of the invention	immunodeficiencies (e.g., as
 (including antibodies and	described below). Additional
agonists or antagonists of the	highly preferred indications
 invention) include the assays	include inflammation and
disclosed in Forrer et al., Biol	inflammatory disorders.
Chem 379(8-9):1101-1110	Highly preferred indications
 (1998); Gupta et al., Exp Cell	also include neoplastic
 Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
Kyriakis JM, Biochem Soc	lymphoma, and/or as described
Symp 64:29-48 (1999); Chang	below under
and Karin, Nature	"Hyperproliferative
410(6824):37-40 (2001); and	Disorders"). Highly preferred
Cobb MH, Prog Biophys Mol	indications include neoplasms
Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
the contents of each of which	lymphoma, prostate, breast,
 are herein incorporated by	lung, colon, pancreatic,
reference in its entirety. T	esophageal, stomach, brain,
cells that may be used	liver, and urinary cancer. Other
according to these assays are	preferred indications include
 publicly available (e.g.,	benign dysproliferative
 through the ATCC).	disorders and pre-neoplastic
Exemplary mouse T cells that	conditions, such as, for
may be used according to these	example, hyperplasia,
assays include the CTLL cell	metaplasia, and/or dvsplasia.

			line, which is an IL-2	Preferred indications include
			dependent suspension-culture	arthritis, asthma, AIDS,
 			cell line with cytotoxic	allergy, anemia, pancytopenia,
			activity.	leukopenia, thrombocytopenia,
				Hodgkin"s disease, acute
				lymphocytic anemia (ALL),
	_			plasmacytomas, multiple
 				myeloma, Burkitt's lymphoma,
				granulomatous disease,
	-			inflammatory bowel disease,
				sepsis, psoriasis, suppression
				of immune reactions to
				transplanted organs and
				tissues, endocarditis,
				meningitis, and Lyme Disease.
HKAABIS	/83	Production of	IFNgamma FMAT. IFNg plays	A highly preferred
		IFNgamma using a	a central role in the immune	embodiment of the invention
		T cells	system and is considered to be	includes a method for
			a proinflammatory cytokine.	stimulating the production of
			IFNg promotes TH1 and	IFNg. An alternative highly
			inhibits TH2 differentiation;	preferred embodiment of the
			promotes IgG2a and inhibits	invention includes a method
	-		IgE secretion; induces	for inhibiting the production of
			macrophage activation; and	IFNg. Highly preferred
			increases MHC expression.	indications include blood
			Assays for immunomodulatory	disorders (e.g., as described
			proteins produced by T cells	below under "Immune
	_		and NK cells that regulate a	Activity", "Blood-Related
			variety of inflammatory	Disorders", and/or
		_	activities and inhibit TH2	"Cardiovascular Disorders"),
			helper cell functions are well	and infection (e.g., viral

infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred
known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160
			_										-	-													-			
										-			-			-											_			
																														,

(2000); G	(2000); Gonzalez et al., J Clin	indications include neoplasms
Lab Anal	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
Billiau et	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
Sci 856:27	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
et al., Anr	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
15:749-75	15:749-795 (1997), and	esophageal, stomach, brain,
Rheumato	Rheumatology (Oxford)	liver and urinary cancer. Other
38(3):214	38(3):214-20 (1999), the	preferred indications include
contents o	contents of each of which are	benign dysproliferative
herein inc	herein incorporated by	disorders and pre-neoplastic
reference	reference in its entirety.	conditions, such as, for
Human T	Human T cells that may be	example, hyperplasia,
nsed acco	used according to these assays	metaplasia, and/or dysplasia.
may be is	may be isolated using	Preferred indications include
technique	techniques disclosed herein or	anemia, pancytopenia,
otherwise	otherwise known in the art.	leukopenia, thrombocytopenia,
Human T	Human T cells are primary	Hodgkin's disease, acute
human lyr	human lymphocytes that	lymphocytic anemia (ALL),
mature in	mature in the thymus and	plasmacytomas, multiple
express a	express a T Cell receptor and	myeloma, Burkitt's lymphoma,
CD3, CD	CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
cells medi	cells mediate humoral or cell-	disease, inflammatory bowel
mediated	mediated immunity and may	disease, sepsis, neutropenia,
be preacti	be preactivated to enhance	neutrophilia, psoriasis,
responsiveness to	ness to	suppression of immune
mounumi	immunomodulatory factors.	reactions to transplanted
		organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
		meningitis, Lyme Disease,
		asthma and allergy.

	HRABA80	784	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred
				routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
_			-	used or routinely modified to	confusion, drowsiness,
				test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,
				cells) by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other
				disclosed in: Shimizu, H., et	diseases and disorders as
				al., Endocr J, 47(3):261-9	described in the
				(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
				Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,

			17 (1000). E:1: V -4-21	no hand die alle and and
			1/ (1999); Filipsson, N., et al.,	endocrine disorders (as
			Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
			(1998); Olson, L.K., et al., J	Disorders" section below),
			Biol Chem, 271(28):16544-52	neuropathy, vision impairment
			(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
			Journal of Biomolecular	blindness), ulcers and impaired
			Screening, 4:193-204 (1999),	wound healing, and infection
			the contents of each of which	(e.g., infectious diseases and
			is herein incorporated by	disorders as described in the
			reference in its entirety.	"Infectious Diseases" section
			Pancreatic cells that may be	below, especially of the
			used according to these assays	urinary tract and skin), carpal
			are publicly available (e.g.,	tunnel syndrome and
 			through the ATCC) and/or	Dupuytren's contracture).
			may be routinely generated.	An additional highly preferred
 			Exemplary pancreatic cells that	indication is obesity and/or
			may be used according to these	complications associated with
			assays include HITT15 Cells.	obesity. Additional highly
			HITT15 are an adherent	preferred indications include
			epithelial cell line established	weight loss or alternatively,
			from Syrian hamster islet cells	weight gain. Additional highly
-	-		transformed with SV40. These	preferred indications are
 			cells express glucagon,	complications associated with
			somatostatin, and	insulin resistance.
-			glucocorticoid receptors. The	
			cells secrete insulin, which is	
		-	stimulated by glucose and	
			glucagon and suppressed by	
			somatostatin or	
 			glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	

				Ashcroff Biochem I 219:	
				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
	HRABA80	784	CD152 in Human T	1007-1010, 1701.	
	HRABA80	787	Agtingtion of	.21	
	IINADAOU	184	Activation of	Kinase assay. Kinase assays,	A highly preferred
			Endothelial Cell	for example an Elk-1 kinase	embodiment of the invention
			ERK Signaling	assay, for ERK signal	includes a method for
			Pathway.	transduction that regulate cell	stimulating endothelial cell
				proliferation or differentiation	growth. An alternative highly
				are well known in the art and	preferred embodiment of the
				may be used or routinely	invention includes a method
				modified to assess the ability	for inhibiting endothelial cell
				of polypeptides of the	growth. A highly preferred
				invention (including antibodies	embodiment of the invention
				and agonists or antagonists of	includes a method for
•				the invention) to promote or	stimulating endothelial cell
				inhibit cell proliferation,	proliferation. An alternative
				activation, and differentiation.	highly preferred embodiment
				Exemplary assays for ERK	of the invention includes a
				kinase activity that may be	method for inhibiting
				used or routinely modified to	endothelial cell proliferation.
				test ERK kinase-induced	A highly preferred
				activity of polypeptides of the	embodiment of the invention
				invention (including antibodies	includes a method for
				and agonists or antagonists of	stimulating apoptosis of
-	•			the invention) include the	endothelial cells. An
				assays disclosed in Forrer et	alternative highly preferred
				al., Biol Chem 379(8-9):1101-	embodiment of the invention
				1110 (1998); Berra et al.,	includes a method for

Bioche	Biochem Pharmacol	inhibiting (e.g., decreasing)
(8)(8):	60(8):1171-1178 (2000);	apoptosis of endothelial cells.
Gupta	Gupta et al., Exp Cell Res	A highly preferred
(247(2)	247(2):495-504 (1999); Chang	embodiment of the invention
and Ka	and Karin, Nature	includes a method for
410(68	410(6824):37-40 (2001); and	stimulating (e.g., increasing)
Copp	Cobb MH, Prog Biophys Mol	endothelial cell activation. An
Biol 7	Biol 71(3-4):479-500 (1999);	alternative highly preferred
the co	the contents of each of which	embodiment of the invention
are her	are herein incorporated by	includes a method for
referen	reference in its entirety.	inhibiting the activation of
Endot	Endothelial cells that may be	(e.g., decreasing) and/or
used a	used according to these assays	inactivating endothelial cells.
are pul	are publicly available (e.g.,	A highly preferred
throug	through the ATCC).	embodiment of the invention
Exemi	Exemplary endothelial cells	includes a method for
that m	that may be used according to	stimulating endothelial cell
these a		differentiation. An alternative
mbili	elial cells	highly preferred embodiment
(HDA)	(HUVEC), which are	of the invention includes a
endoth	endothelial cells which line	method for inhibiting
venous	venous blood vessels, and are	endothelial cell differentiation.
vlovni	involved in functions that	A highly preferred
includ	include, but are not limited to,	embodiment of the invention
angiog	angiogenesis, vascular	includes a method for
berme	permeability, vascular tone,	stimulating angiogenisis. An
and im	and immune cell extravasation.	alternative highly preferred
		embodiment of the invention
		includes a method for
		inhibiting angiogenesis.
		A highly preferred

		embodiment of the invention
 		includes a method for reducing
_		cardiac hypertrophy. An
		alternative highly preferred
		embodiment of the invention
		.=
		cardiac hypertrophy. Highly
		☲
 		neoplastic diseases (e.g., as
		described below under
		"Hyperproliferative
		Disorders"), and disorders of
		the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
		aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
		and atherosclerotic vascular
,		disease, diabetic nephropathy,
		intracardiac shunt, cardiac
		hypertrophy, myocardial
		infarction, chronic
		hemodynamic overload, and/or
 		as described below under
-		"Cardiovascular Disorders").
		Highly preferred indications
 		include cardiovascular,
 		endothelial and/or angiogenic
		disorders (e.g., systemic

prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and
				-																										
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	_																													

atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal	diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinonathies, thrombetic	and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis	and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g.

				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
		_		below) and
			٠	immunodeficiencies (e.g., as
				described below). Additional
				preferred indications include
				inflammation and
				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
			(and Crohn's disease), and pain
	,			management.
HRACD15	785	Regulation of	Assays for the regulation of	A highly preferred
		transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
		Malic Enzyme in	are well-known in the art and	An additional highly preferred
	-	hepatocytes	may be used or routinely	indication is a complication
			modified to assess the ability	associated with diabetes (e.g.,
			of polypeptides of the	diabetic retinopathy, diabetic
			invention (including antibodies	nephropathy, kidney disease
	-		and agonists or antagonists of	(e.g., renal failure,
			the invention) to regulate	nephropathy and/or other
			transcription of Malic Enzyme,	diseases and disorders as
			a key enzyme in lipogenesis.	described in the "Renal
			Malic enzyme is involved in	Disorders" section below),
			lipogenesisand its expression is	diabetic neuropathy, nerve
			stimulted by insulin. ME	disease and nerve damage
			promoter contains two direct	(e.g., due to diabetic
			repeat (DR1)- like elements	neuropathy), blood vessel
			MEp and MEd identified as	blockage, heart disease, stroke,

	putative PPAR response	impotence (e.g., due to diabetic
	elements. ME promoter may	neuropathy or blood vessel
	also responds to AP1 and other	blockage), seizures, mental
	transcription factors.	confusion, drowsiness,
-	Exemplary assays that may be	nonketotic hyperglycemic-
	used or routinely modified to	hyperosmolar coma,
	test for regulation of	cardiovascular disease (e.g.,
	transcription of Malic Enzyme	heart disease, atherosclerosis,
	(in hepatocytes) by	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in: Streeper, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	Disorders" section below),
	Endocrinol, 8(10):1361-9	neuropathy, vision impairment
	(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
	Biol Chem, 274(25):17997-	blindness), ulcers and impaired
	8004 (1999); Ijpenberg, A., et	wound healing, and infection
	al., J Biol Chem,	(e.g., infectious diseases and
	272(32):20108-20117 (1997);	disorders as described in the
	Berger, et al., Gene 66:1-10	"Infectious Diseases" section
	(1988); and, Cullen, B., et al.,	below, especially of the
	Methods in Enzymol.	urinary tract and skin), carpal
	216:362–368 (1992), the	tunnel syndrome and
	contents of each of which is	Dupuytren's contracture).
	herein incorporated by	An additional highly preferred
	reference in its entirety.	indication is obesity and/or
	Hepatocytes that may be used	complications associated with

			according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays includes the mouse 3T3-L1 is a mouse preadipocyte cell line (adherent). It is a continuous substrain of 3T3 fibroblasts developed through clonal isolation. Cells undergo a preadipocyte to adipose-like conversion under appropriate differentiation culture	obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
HRACD15	785	Activation of T-Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation, activation, and apoptosis.	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders", blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include

	Exemplary assays for JNK and	autoimmine diseases (e o
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,
	are herein incorporated by	lung, colon, pancreatic,
	reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver, and urinary cancer. Other
	according to these assays are	preferred indications include
	publicly available (e.g.,	benign dysproliferative
	through the ATCC).	disorders and pre-neoplastic
	Exemplary mouse T cells that	conditions, such as, for
	may be used according to these	example, hyperplasia,
	assays include the CTLL cell	metaplasia, and/or dysplasia.
-	line, which is an IL-2	Preferred indications include
	dependent suspension-culture	arthritis, asthma, AIDS,

HRACD15 785 SEAP in HIB/CRE activity. HRACD15 785 Regulation of Caspase apoptosis of immune cells (such known in as mast cells). assess the polypepti (including agonists of invention protease-immune cells and muco the body, the body,	allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningits, and I vme Disease	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of apolypeptides of the invention polypeptides of the invention polypeptides of the invention agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation
	cell line v activity.	f f s (such
HRACD15		785
		HRACD15 HRACD15

cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000); Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by	reference in its entirety.	Immune cells that may be used	according to these assays are	publicly available (e.g.,
																		_												
																													-	

				through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	
工。	HRACD15	785	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)		
H	HRACJ35	786	Regulation of transcription of Malic Enzyme in	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and	A highly preferred indication is diabetes mellitus. An additional highly preferred
			hepatocytes	may be used or routinely modified to assess the ability	indication is a complication associated with diabetes (e.g.,
				or polypeptides of the invention (including antibodies and agonists or antagonists of	diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure,
				the invention) to regulate transcription of Malic Enzyme,	nephropathy and/or other diseases and disorders as
				a key enzyme in lipogenesis. Malic enzyme is involved in linogenesisand its expression is	described in the "Kenal Disorders" section below), disheric neuronathy, nerve
				stimulted by insulin. ME promoter contains two direct	disease and nerve damage (e.g., due to diabetic
				repeat (DR1)- like elements MEp and MEd identified as	neuropathy), blood vessel blockage, heart disease, stroke,
				putative PPAR response elements. ME promoter may	impotence (e.g., due to diabetic neuropathy or blood vessel
	-			also responds to AP1 and other transcription factors.	blockage), seizures, mental
				Exemplary assays that may be	nonketotic hyperglycemic-

may be used according to these assays includes the mouse 3T3-L1 cell line. 3T3-L1 is a mouse preadipocyte cell line (adherent). It is a continuous substrain of 3T3 fibroblasts developed through clonal isolation. Cells undergo a preadipocyte to adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	Production of Assays for measuring CAM in expression of VCAM are well-endothelial cells known in the art and may be endothelial cells known in the art and may be and chronic), restnosis, used or routinely modified to assess the ability of allergy. Highly preferred including antibodies and inflammation and agonists or antagonists of the invention to regulate VCAM invention) to regulate VCAM invention of cell surface cardiovascular disorders (such VCAM-1 expression in endothelial cells. Endothelial cells. Endothelial cells and are involved in functions that include, but are and/or "Cardiovascular includes." Highly preferred indications as described below under endothelial cells. Endothelial cells are cells that line blood related Disorders." Highly preferred indications that include, but are objected in disorders. Highly preferred indications that include, but are objected indications.
	786
	HRACJ35

			tone, and immune cell	and cancers such as, for
			endothelial cells that may be	melanoma, renal cell
			used according to these assays	carcinoma, and prostate,
			include human umbilical vein	breast, lung, colon, pancreatic,
			endothelial cells (HUVEC),	esophageal, stomach, brain,
			which are available from	liver and urinary cancer. Other
			commercial sources. The	preferred indications include
			expression of VCAM	benign dysproliferative
			(CD106), a membrane-	disorders and pre-neoplastic
			associated protein, can be	conditions, such as, for
			upregulated by cytokines or	example, hyperplasia,
			other factors, and contributes	metaplasia, and/or dysplasia.
		-	to the extravasation of	
			lymphocytes, leucocytes and	
			other immune cells from blood	
			vessels; thus VCAM	
			expression plays a role in	
			promoting immune and	
			inflammatory responses.	
HRACJ35	786	Hexosaminidase in		
		RBL-2H3		
HRDFD27	787	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
,		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha

			antagonists of the invention) to	production. Preferred
			aming of mine of the community of the co	2
		-	regulare inc sermin response	disorders (e a se described
			lactors and modulate me	uisoliucis (c.g.; as ucsciiocu
			expression of genes involved	below under "Immune
			in growth. Exemplary assays	Activity", "Blood-Related
			for transcription through the	Disorders", and/or
_			SRE that may be used or	"Cardiovascular Disorders"),
			routinely modified to test SRE	Highly preferred indications
			activity of the polypeptides of	include autoimmune diseases
	-		the invention (including	(e.g., rheumatoid arthritis,
			antibodies and agonists or	systemic lupus erythematosis,
			antagonists of the invention)	Crohn"s disease, multiple
			include assays disclosed in	sclerosis and/or as described
			Berger et al., Gene 66:1-10	below), immunodeficiencies
			(1998); Cullen and Malm,	(e.g., as described below),
			Methods in Enzymol 216:362-	boosting a T cell-mediated
			368 (1992); Henthorn et al.,	immune response, and
			Proc Natl Acad Sci USA	suppressing a T cell-mediated
			85:6342-6346 (1988); and	immune response. Additional
			Black et al., Virus Genes	highly preferred indications
			12(2):105-117 (1997), the	include inflammation and
			content of each of which are	inflammatory disorders, and
			herein incorporated by	treating joint damage in
			reference in its entirety. T	patients with rheumatoid
			cells that may be used	arthritis. An additional highly
-			according to these assays are	preferred indication is sepsis.
			publicly available (e.g.,	Highly preferred indications
			through the ATCC).	include neoplastic diseases
			Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
			may be used according to these	and/or as described below
			assays include the CTLL cell	under "Hyperproliferative

				hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HRDFD27	787	IL-10 in Human T- cell 2B9		
HRDFD27	787	Activation of Endothelial Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation.
			activity of polypeptides of the invention (including antibodies	embodiment of the invention includes a method for

stimulating apoptosis of endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing) the	activation of and/or	inactivating endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment
and agonists or antagonists of the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.
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																-							•						

of the invention includes a method for inducing cardiac hypertrophy. Highly	preferred indications include neoplastic diseases (e.g., as	described below under "Hyperproliferative Disorders"), and disorders of	the cardiovascular system (e.g., heart disease, congestive	heart failure, hypertension, aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the

arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangiopericytoma, haemangiopericytoma,
lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred

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indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	schemia reperfusion injury,	rhenmatoid arthritis
ipui	dys	pre-	as, 1	met	Hig	also	snc	hyp	dise	vasc	dise	bhei	reste	lym	thro	lym]	lym]	vasc	perij	and	pref	inch	mom	tissn	snch	ballc	athe	ldmi	ische	rhei
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		cere	cerebrovascular disease, renal
		dise	diseases such as acute renal
		fail	failure, and osteoporosis.
		Ade	Additional highly preferred
		ibui	indications include stroke,
		grai	graft rejection, diabetic or
		othe	other retinopathies, thrombotic
•		and	and coagulative disorders,
		Vas	vascularitis, lymph
		ang	angiogenesis, sexual disorders,
		age	age-related macular
-		deg	degeneration, and treatment
	_	/pre	/prevention of endometriosis
		and	and related conditions.
		Ade	Additional highly preferred
		indi	indications include fibromas,
		hea	heart disease, cardiac arrest,
		hea	heart valve disease, and
		Vas	vascular disease.
	-	Prej	Preferred indications include
		bloc	blood disorders (e.g., as
		qese	described below under
		mI,,	"Immune Activity", "Blood-
		Rel	Related Disorders", and/or
			"Cardiovascular Disorders").
		Pre	Preferred indications include
	-	autc	autoimmune diseases (e.g.,
		rhen	rheumatoid arthritis, systemic
		ldul	lupus erythematosis, multiple
		scle	sclerosis and/or as described
		belc	below) and

				immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and
,				inflammatory disorders (such as acute and chronic
				inflammatory diseases, e.g.,
				and Crohn's disease), and pain
				management.
787	V	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include inflammation and
	==	through NFKB	NFKB response element are	inflammatory disorders.
	<u> </u>	response element in	well-known in the art and may	Highly preferred indications
	<u></u>	immune cells (such	be used or routinely modified	include blood disorders (e.g.,
	<u> </u>	as natural killer	to assess the ability of	as described below under
	<u> </u>	cells).	polypeptides of the invention	"Immune Activity", "Blood-
	-		(including antibodies and	Related Disorders", and/or
			agonists or antagonists of the	"Cardiovascular Disorders").
			invention) to regulate NFKB	Highly preferred indications
	-		transcription factors and	include autoimmune diseases
-			modulate expression of	(e.g., rheumatoid arthritis,
		,	immunomodulatory genes.	systemic lupus erythematosis,
			Exemplary assays for	multiple sclerosis and/or as
		<u></u>	transcription through the	described below), and
	-		NFKB response element that	immunodeficiencies (e.g., as
			may be used or rountinely	described below). An
		_	modified to test NFKB-	additional highly preferred
	_	-	response element activity of	indication is infection (e.g.,
			polypeptides of the invention	AIDS, and/or an infectious
			(including antibodies and	disease as described below

	agonists or antagonists of the	under "Infectious Disease")
	invention) include assays	Highly preferred indications
	disclosed in Berger et al., Gene	include neoplastic diseases
	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
	Malm, Methods in Enzymol	lymphoma, and/or as described
	216:362-368 (1992); Henthorn	below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85:6342-6346 (1988); Valle	Disorders"). Highly preferred
	Blazquez et al, Immunology	indications include neoplasms
	90(3):455-460 (1997);	and cancers, such as, for
	Aramburau et al., J Exp Med	example, melanoma, renal cell
	82(3):801-810 (1995); and	carcinoma, leukemia,
-	Fraser et al., 29(3):838-844	lymphoma, and prostate,
	(1999), the contents of each of	breast, lung, colon, pancreatic,
	which are herein incorporated	esophageal, stomach, brain,
	by reference in its entirety.	liver and urinary cancer. Other
	NK cells that may be used	preferred indications include
	according to these assays are	benign dysproliferative
-	publicly available (e.g.,	disorders and pre-neoplastic
	through the ATCC).	conditions, such as, for
	Exemplary human NK cells	example, hyperplasia,
	that may be used according to	metaplasia, and/or dysplasia.
	these assays include the NKL	Preferred indications also
	cell line, which is a human	include anemia, pancytopenia,
	natural killer cell line	leukopenia, thrombocytopenia,
	established from the peripheral	Hodgkin's disease, acute
	blood of a patient with large	lymphocytic anemia (ALL),
	granular lymphocytic	plasmacytomas, multiple
	leukemia. This IL-2 dependent	myeloma, Burkitt's lymphoma,
	suspension culture cell line has	arthritis, AIDS, granulomatous
	a morphology resembling that	disease, inflammatory bowel

				of activated NK cells.	disease sensis neutronenia
					neutrophilia, psoriasis,
_					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
	-				meningitis, Lyme Disease,
		-			suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HRGBL78	788	Stimulation of	Assays for measuring secretion	A highly preferred
			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication
	•			the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
•				used or routinely modified to	confusion, drowsiness,
				test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,

	cells) by polynentides of the	cardiovascular disease (e.g.
	invention (including antibodies	heart disease, atherosclerosis
	and agonists or antagonists of	microvascular disease
-	the invention) include assays	hypertension, stroke, and other
	disclosed in: Ahren, B., et al.,	diseases and disorders as
	Am J Physiol, 277(4 Pt	described in the
	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
	al., Endocrinology,	section below), dyslipidemia,
	138(9):3735-40 (1997); Kim,	endocrine disorders (as
	K.H., et al., FEBS Lett,	described in the "Endocrine
	377(2):237-9 (1995); and,	Disorders" section below),
	Miraglia S et. al., Journal of	neuropathy, vision impairment
	Biomolecular Screening,	(e.g., diabetic retinopathy and
	4:193-204 (1999), the contents	blindness), ulcers and impaired
	of each of which is herein	wound healing, and infection
	incorporated by reference in its	(e.g., infectious diseases and
	entirety. Pancreatic cells that	disorders as described in the
	may be used according to these	"Infectious Diseases" section
	assays are publicly available	below, especially of the
	(e.g., through the ATCC)	urinary tract and skin), carpal
	and/or may be routinely	tunnel syndrome and
	generated. Exemplary	Dupuytren's contracture).
	pancreatic cells that may be	An additional highly preferred
	used according to these assays	indication is obesity and/or
	include rat INS-1 cells. INS-1	complications associated with
	cells are a semi-adherent cell	obesity. Additional highly
	line established from cells	preferred indications include
	isolated from an X-ray induced	weight loss or alternatively,
	rat transplantable insulinoma.	weight gain. Aditional
	These cells retain	highly preferred indications are
	characteristics typical of native	complications associated with

			pancreatic beta cells including	insulin resistance.
			glucose inducible insulin	
			secretion. References: Asfari	
			et al. Endocrinology 1992 130:167.	
HROAJ03	789	IL-4 in HMC		
HROAJ03	789	Activation of	Kinase assay. JNK and p38	A highly preferred
		Endothelial Cell	kinase assays for signal	embodiment of the invention
		p38 or JNK	transduction that regulate cell	includes a method for
	-	Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
			apoptosis are well known in	growth. An alternative highly
			the art and may be used or	preferred embodiment of the
			routinely modified to assess	invention includes a method
			the ability of polypeptides of	for inhibiting endothelial cell
			the invention (including	growth. A highly preferred
			antibodies and agonists or	embodiment of the invention
			antagonists of the invention) to	includes a method for
	<i>,</i> .		promote or inhibit cell	stimulating endothelial cell
			proliferation, activation, and	proliferation. An alternative
			apoptosis. Exemplary assays	highly preferred embodiment
			for JNK and p38 kinase	of the invention includes a
			activity that may be used or	method for inhibiting
			routinely modified to test JNK	endothelial cell proliferation.
			and p38 kinase-induced	A highly preferred
			activity of polypeptides of the	embodiment of the invention
			invention (including antibodies	includes a method for
			and agonists or antagonists of	stimulating apoptosis of
			the invention) include the	endothelial cells. An
			assays disclosed in Forrer et	alternative highly preferred
			al., Biol Chem 379(8-9):1101-	embodiment of the invention
			1110 (1998); Gupta et al., Exp	includes a method for

	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
-	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	Exemplary endothelial cells	embodiment of the invention
	that may be used according to	includes a method for
	these assays include human	stimulating angiogenisis. An
	umbilical vein endothelial cells	alternative highly preferred
	(HUVEC), which are	embodiment of the invention
	endothelial cells which line	includes a method for
	venous blood vessels, and are	inhibiting angiogenesis. A
	involved in functions that	highly preferred embodiment
	include, but are not limited to,	of the invention includes a
	angiogenesis, vascular	method for reducing cardiac
	permeability, vascular tone,	hypertrophy. An alternative
	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as

_																														
described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly
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		preferred are indications that
		intitit and indications that
		innibit anglogenesis and/or
		cardiovascularization.
		Highly preferred indications
		include antiangiogenic activity
		to treat solid tumors,
		leukemias, and Kaposi"s
		sarcoma, and retinal disorders.
		Highly preferred indications
-		include neoplasms and cancer,
		such as, Kaposi"s sarcoma,
		hemangioma (capillary and
		cavernous), glomus tumors,
		telangiectasia, bacillary
	 ,	angiomatosis,
		hemangioendothelioma,
		angiosarcoma,
		haemangiopericytoma,
		lymphangioma,
		lymphangiosarcoma. Highly
		preferred indications also
		include cancers such as,
		prostate, breast, lung, colon,
		pancreatic, esophageal,
		stomach, brain, liver, and
		urinary cancer. Preferred
		indications include benign
		dysproliferative disorders and
		pre-neoplastic conditions, such
		as, for example, hyperplasia,
		metaplasia, and/or dysplasia.

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Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke.
												-												Para						
					-								_		_									_						
																	-				_								-	

graft reject	graft rejection, diabetic or
other retinc	other retinopathies, thrombotic
and coaguli	and coagulative disorders,
 vascularitis, lymph	s, lymph
 angiogenes	angiogenesis, sexual disorders,
 age-related macular	l macular
 degeneratio	degeneration, and treatment
/prevention	/prevention of endometriosis
and related	and related conditions.
Additional	Additional highly preferred
 indications	indications include fibromas,
 heart diseas	heart disease, cardiac arrest,
 heart valve	heart valve disease, and
 vascular disease.	sease.
 Preferred in	Preferred indications include
blood disor	blood disorders (e.g., as
 described b	described below under
"Immune A	"Immune Activity", "Blood-
 Related Dis	Related Disorders", and/or
 "Cardiovas	"Cardiovascular Disorders").
Preferred in	Preferred indications include
autoimmun	autoimmune diseases (e.g.,
rheumatoid	rheumatoid arthritis, systemic
lupus eryth	lupus erythematosis, multiple
 sclerosis an	sclerosis and/or as described
below) and	
 immunodef	immunodeficiencies (e.g., as
described b	described below). Additional
 preferred in	preferred indications include
inflammation and	on and
inflammato	inflammatory disorders (such

				as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
HROAJ39	790	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular factors can cause an influx of calcium, leading to activation of calcium, leading to activation of calcium, responsive signaling pathways and alterations in cell	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental
			that may be used or routinely modified to measure calcium flux by polypeptides of the	nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g.,
			invention (including antibodies and agonists or antagonists of	heart disease, atherosclerosis, microvascular disease,

	4	the invention) include assays	hypertension, stroke, and other
	- -	disclosed in: Satin LS, et al.,	diseases and disorders as
		Endocrinology, 136(10):4589-	described in the
	9	601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
	<u> </u>	Endocrinology, 136(7):2960-6	section below), dyslipidemia,
	(1)	(1995); Richardson SB, et al.,	endocrine disorders (as
-	B	Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
	(1)	(1992); and, Meats, JE, et al.,	Disorders" section below),
		Cell Calcium 1989 Nov-	neuropathy, vision impairment
	Ω	Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
	3	contents of each of which is	blindness), ulcers and impaired
	he	herein incorporated by	wound healing, and infection
	re	reference in its entirety.	(e.g., infectious diseases and
	P	Pancreatic cells that may be	disorders as described in the
	sn	used according to these assays	"Infectious Diseases" section
	ar	are publicly available (e.g.,	below, especially of the
	th	through the ATCC) and/or	urinary tract and skin), carpal
	m _	may be routinely generated.	tunnel syndrome and
-	<u> </u>	Exemplary pancreatic cells that	Dupuytren's contracture).
	<u>u</u>	may be used according to these	An additional highly preferred
	as	assays include HITT15 Cells.	indication is obesity and/or
	H	HITT15 are an adherent	complications associated with
	ia	epithelial cell line established	obesity. Additional highly
	- Î	from Syrian hamster islet cells	preferred indications include
	tra	transformed with SV40. These	weight loss or alternatively,
	90	cells express glucagon,	weight gain. Aditional
	SC	somatostatin, and	highly preferred indications are
	lg	glucocorticoid receptors. The	complications associated with
	90	cells secrete insulin, which is	insulin resistance.
	st	stimulated by glucose and	
	g	glucagon and suppressed by	

			somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	
HROBD68	791	Regulation of apoptosis in pancreatic beta	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a second control of the preferred
		cells.	assess the ability of polypeptides of the invention (including antibodies and	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease
			agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis.	(e.g., renal failure, nephropathy and/or other diseases and disorders as
			Apoptosis in pancreatic beta is associated with induction and progression of diabetes.	described in the "Renal Disorders" section below), diabetic neuropathy, nerve
			exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of	disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,
			polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays	impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,
			disclosed in: Loweth, AC, et al., FEBS Lett, 400(3):285-8 (1997); Saini, KS, et al.,	nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g.,

	Biochem Mol Biol Int.	heart disease, atherosclerosis.
	 39(6):1229-36 (1996);	microvascular disease.
	 Krautheim, A., et al., Br J	hypertension, stroke, and other
	Pharmacol, 129(4):687-94	diseases and disorders as
	 (2000); Chandra J, et al.,	described in the
	Diabetes, 50 Suppl 1:S44-7	"Cardiovascular Disorders"
	(2001); Suk K, et al., J	section below), dyslipidemia,
	 Immunol, 166(7):4481-9	endocrine disorders (as
	 (2001); Tejedo J, et al., FEBS	described in the "Endocrine
	 Lett, 459(2):238-43 (1999);	Disorders" section below),
	 Zhang, S., et al., FEBS Lett,	neuropathy, vision impairment
	455(3):315-20 (1999); Lee et	(e.g., diabetic retinopathy and
	 al., FEBS Lett 485(2-3): 122-	blindness), ulcers and impaired
	 126 (2000); Nor et al., J Vasc	wound healing, and infection
	Res 37(3): 209-218 (2000);	(e.g., infectious diseases and
	and Karsan and Harlan, J	disorders as described in the
	Atheroscler Thromb 3(2): 75-	"Infectious Diseases" section
	80 (1996); the contents of each	below, especially of the
	of which are herein	urinary tract and skin), carpal
	incorporated by reference in its	tunnel syndrome and
	 entirety. Pancreatic cells that	Dupuytren's contracture).
	may be used according to these	An additional highly preferred
	 assays are publicly available	indication is obesity and/or
	(e.g., through the ATCC)	complications associated with
	and/or may be routinely	obesity. Additional highly
_	generated. Exemplary	preferred indications include
	 pancreatic cells that may be	weight loss or alternatively,
	 used according to these assays	weight gain. Aditional
	 include RIN-m. RIN-m is a	highly preferred indications are
	 rat adherent pancreatic beta	complications associated with
	cell insulinoma cell line	insulin resistance.

			derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980 77:3519.	
HSATR82	792	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications
			activity of the polypeptides of the invention (including antibodies and agonists or	include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,

ant	antagonists of the invention)	Crohn"s disease, multiple
 inc	include assays disclosed in	sclerosis and/or as described
Bel	Berger et al., Gene 66:1-10	below), immunodeficiencies
(19	(1998); Cullen and Malm,	(e.g., as described below),
Me	Methods in Enzymol 216:362-	boosting a T cell-mediated
 398	368 (1992); Henthorn et al.,	immune response, and
 Pro	Proc Natl Acad Sci USA	suppressing a T cell-mediated
85:	85:6342-6346 (1988); and	immune response. Additional
 Bla	Black et al., Virus Genes	highly preferred indications
 12(12(2):105-117 (1997), the	include inflammation and
 con	content of each of which are	inflammatory disorders, and
her	herein incorporated by	treating joint damage in
 refe	reference in its entirety. T	patients with rheumatoid
 llao	cells that may be used	arthritis. An additional highly
 acc	according to these assays are	preferred indication is sepsis.
and	publicly available (e.g.,	Highly preferred indications
 thre	through the ATCC).	include neoplastic diseases
Exe	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
 ma	may be used according to these	and/or as described below
ass	assays include the CTLL cell	under "Hyperproliferative
 line	line, which is an IL-2	Disorders"). Additionally,
 dep	dependent suspension culture	highly preferred indications
 Jo	of T cells with cytotoxic	include neoplasms and
acti	activity.	cancers, such as, for example,
 		leukemia, lymphoma,
 		melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
 		lung, colon, pancreatic,
 		esophageal, stomach, brain,
		liver and urinary cancer. Other

benign dysptoliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukopenia, thrombocytopenia, leukopenia, thrombocytopenia, leukopenia, thrombocytopenia, leukopenia, sissase, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitr's lymphon arthritis, AIDS, granulomato disease, inflammatory bowel disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulatio diabetes mellitus, endocardit meningitis, Lyme Disease, cardiac reperfusion injury, an asthma and allergy. An additional preferred indicatic is infection (e.g., an infection disease as described below under "Infectious Disease").			preferred indications include
ausoracis and pre-neople conditions, such as, for example, hyperplasia, metaplasia, and/or dysp Preferred indications in anemia, pancytopenia, leukopenia, thrombocyt Hodgkin's disease, acut lymphocytic anemia (A plasmacytomas, multip myeloma, Burkit's lym arthritis, AIDS, granulc disease, inflammatory the disease, inflammatory disease, inflamma			benign dysproliterative
example, hyperplasia, metaplasia, andror dysp Preferred indications in anemia, pancytopenia, leukopenia, thrombocyt Hodgkin's disease, acul lymphocytic anemia (A plasmacytomas, multip myeloma, Burkitt's lymarthritis, AIDS, granulc disease, inflammatory the disease, inflammatory disease, inflammatory disease, inflammatory disease, inflammatory disease, neutrophilia, psoriasis, suppression of immune reactions to transplante organs and tissues, hemophilia, hypercoagn diabetes mellitus, endomeningitis, Lyme Diseccardiac reperfusion injuasthma and allergy. additional preferred ind is infection (e.g., an inf disease as described be under "Infectious Disecunder" "Infectious Disec			disorders and pre-neoplastic
metaplasia, and/or dysp Preferred indications in anemia, pancytopenia, leukopenia, thrombocyt Hodgkin's disease, acul lymphocytic anemia (A plasmacytomas, multip myeloma, Burkitt's lyr arthritis, AIDS, granulo disease, inflammatory t disease as described be under "Infectious Disee			example, hyperplasia,
Preferred indications in anemia, pancytopenia, leukopenia, thrombocyt Hodgkin's disease, acul lymphocytic anemia (A plasmacytomas, multip myeloma, Burkitt's lyrr arthritis, AIDS, granulo disease, inflammatory the disease, inflammatory the disease, inflammatory the disease, inflammatory the disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplante organs and tissues, hemophilia, hypercoagu diabetes mellitus, endon meningitis, Lyme Disea cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an infi disease as described be under "Infectious Disea under "Infectious Disea			metaplasia, and/or dysplasia.
anemia, pancytopenia, leukopenia, thrombocyt Hodgkin's disease, acut lymphocytic anemia (A plasmacytomas, multip myeloma, Burkitt's lyrr arthritis, AIDS, granulo disease, inflammatory the disease, inflammatory the disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplante organs and tissues, hemophilia, hypercoaga diabetes mellitus, endor meningitis, Lyme Disea cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an inf disease as described be under "Infectious Disea		•	Preferred indications include
leukopenia, thrombocyt Hodgkin's disease, acut lymphocytic anemia (A plasmacytomas, multip myeloma, Burkitt's lym arthritis, AIDS, granulo disease, inflammatory t disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplante organs and tissues, hemophilia, hypercoagd diabetes mellitus, endo meningitis, Lyme Dise cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an inf disease as described be under "Infectious Dises			anemia, pancytopenia,
Hodgkin's disease, acul lymphocytic anemia (A plasmacytomas, multipl myeloma, Burkitt's lyrr arthritis, AIDS, granulo disease, inflammatory the disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplante organs and tissues, hemophilia, hypercoagu diabetes mellitus, endor meningitis, Lyme Disease cardiac reperfusion injustitum and allergy. additional preferred ind is infection (e.g., an infidisease as described be under "Infectious Disease under "Infectious Disease").			leukopenia, thrombocytopenia,
lymphocytic anemia (A plasmacytomas, multipl myeloma, Burkitt's lym arthritis, AIDS, granulo disease, inflammatory t disease, inflammatory t disease, inflammatory t disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplante organs and tissues, hemophilia, hypercoagu diabetes mellitus, endor meningitis, Lyme Diseasthma and allergy. asthma and allergy. additional preferred ind is infection (e.g., an inf disease as described be under "Infectious Diseasured".			Hodgkin's disease, acute
plasmacytomas, multipl myeloma, Burkitt's lym arthritis, AIDS, granulo disease, inflammatory the disease, inflammatory the disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplante organs and tissues, hemophilia, hypercoagu diabetes mellitus, endor meningitis, Lyme Diseacardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an infi disease as described be under "Infectious Diseaunder" "Infectious "Infectious Diseaunder" "Infectious "I			lymphocytic anemia (ALL),
myeloma, Burkitt's lym arthritis, AIDS, granulo disease, inflammatory t disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplante organs and tissues, hemophilia, hypercoagu diabetes mellitus, endo meningitis, Lyme Dise cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an inf disease as described be under "Infectious Dises			plasmacytomas, multiple
arthritis, AIDS, granulo disease, inflammatory b disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplante organs and tissues, hemophilia, hypercoagu diabetes mellitus, endo meningitis, Lyme Disea cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an inf disease as described be under "Infectious Disea	-		myeloma, Burkitt's lymphoma,
disease, inflammatory b disease, neutrophilia, psoriasis, suppression of immune reactions to transplante organs and tissues, hemophilia, hypercoagn diabetes mellitus, endor meningitis, Lyme Disea cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an inf disease as described be under "Infectious Disea		-	arthritis, AIDS, granulomatous
disease, neutrophila, neutrophila, psoriasis, suppression of immune reactions to transplante organs and tissues, hemophilia, hypercoagi diabetes mellitus, endor meningitis, Lyme Disec cardiac reperfusion injuasthma and allergy. additional preferred ind is infection (e.g., an infersions Disec under "Infectious Disecurdes")			disease, inflammatory bowel
neutrophilia, psoriasis, suppression of immune reactions to transplanteo organs and tissues, hemophilia, hypercoagu diabetes mellitus, endo meningitis, Lyme Disec cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an inf disease as described be under "Infectious Dises under "Infectious Dises			disease, neutropenia,
suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagu diabetes mellitus, endor meningitis, Lyme Disea cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an inf disease as described be under "Infectious Dises			neutrophilia, psoriasis,
reactions to transplanted organs and tissues, hemophilia, hypercoagu diabetes mellitus, endor meningitis, Lyme Disec cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an infection (e.g., an infections Disec under "Infectious Dises under "Infectious Dises			suppression of immune
organs and tissues, hemophilia, hypercoagu diabetes mellitus, endoc meningitis, Lyme Dises cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an inf disease as described be under "Infectious Dises			reactions to transplanted
hemophilia, hypercoaga diabetes mellitus, endoc meningitis, Lyme Dises cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an infection (e.g., an infection disease as described belunder "Infectious Dises under "Infectious Dises			organs and tissues,
diabetes mellitus, endoc meningitis, Lyme Disez cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an inf disease as described bel under "Infectious Disez			hemophilia, hypercoagulation,
meningitis, Lyme Disea cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an inf disease as described belunder "Infectious Disea			diabetes mellitus, endocarditis,
cardiac reperfusion inju asthma and allergy. additional preferred ind is infection (e.g., an infection (e.g., an infections Dises under "Infectious Dises			meningitis, Lyme Disease,
additional preferred ind is infection (e.g., an infection disease as described be under "Infectious Dises			cardiac reperfusion injury, and
additional preferred ind is infection (e.g., an infection (e.g., an infection disease as described belonder "Infectious Disease as described belonder".			asthma and allergy. An
is infection (e.g., an infection disease as described belander "Infectious Disease"			additional preferred indication
disease as described bel under "Infectious Disease"			is infection (e.g., an infectious
under "Infectious Disea			disease as described below
			under "Infectious Disease").
Kinase assay. JNK and p38		Kinase assay. JNK and p38	Preferred indications include
Cell p38 or JNK kinase assays for signal neoplastic diseases (e.g.	Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as

	Signaling Pathway.	transduction that regulate cell	described below under
		proliferation, activation, or	"Hyperproliferative
		apoptosis are well known in	Disorders"), blood disorders
		the art and may be used or	(e.g., as described below under
		routinely modified to assess	"Immune Activity",
		the ability of polypeptides of	"Cardiovascular Disorders",
		the invention (including	and/or "Blood-Related
		antibodies and agonists or	Disorders"), and infection
		antagonists of the invention) to	(e.g., an infectious disease as
		promote or inhibit immune cell	described below under
		(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
		activation, and apoptosis.	preferred indications include
-		Exemplary assays for JNK and	autoimmune diseases (e.g.,
		p38 kinase activity that may be	rheumatoid arthritis, systemic
		used or routinely modified to	lupus erythematosis, multiple
		test JNK and p38 kinase-	sclerosis and/or as described
		induced activity of	below) and
-		polypeptides of the invention	immunodeficiencies (e.g., as
		(including antibodies and	described below). Additional
		agonists or antagonists of the	highly preferred indications
		invention) include the assays	include inflammation and
		disclosed in Forrer et al., Biol	inflammatory disorders.
		Chem 379(8-9):1101-1110	Highly preferred indications
		(1998); Gupta et al., Exp Cell	also include neoplastic
		Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
		Kyriakis JM, Biochem Soc	lymphoma, and/or as described
_	-	Symp 64:29-48 (1999); Chang	below under
		and Karin, Nature	"Hyperproliferative
		410(6824):37-40 (2001); and	Disorders"). Highly preferred
		Cobb MH, Prog Biophys Mol	indications include neoplasms
		Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,

	the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these	lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hymeralasia
	assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
ICAM in Normal Human Bronchial Epitheliae		
IL-8 in Normal Human Bronchial Epitheliae		

HSAWD74	794	Regulation of	Assays for the regulation of	A highly preferred indication
		transcription via	transcription throlloh the	is diabetes mellitus
		DMEF1 response	DMEF1 response element are	Additional highly preferred
		element in	well-known in the art and may	indications include
		adipocytes and pre-	be used or routinely modified	complications associated with
		adipocytes	to assess the ability of	diabetes (e.g., diabetic
			polypeptides of the invention	retinopathy, diabetic
			(including antibodies and	nephropathy, kidney disease
			agonists or antagonists of the	(e.g., renal failure,
			invention) to activate the	nephropathy and/or other
			DMEF1 response element in a	diseases and disorders as
			reporter construct (such as that	described in the "Renal
			containing the GLUT4	Disorders" section below),
			promoter) and to regulate	diabetic neuropathy, nerve
			insulin production. The	disease and nerve damage
			DMEF1 response element is	(e.g., due to diabetic
			present in the GLUT4	neuropathy), blood vessel
			promoter and binds to MEF2	blockage, heart disease, stroke,
			transcription factor and another	impotence (e.g., due to diabetic
			transcription factor that is	neuropathy or blood vessel
			required for insulin regulation	blockage), seizures, mental
			of Glut4 expression in skeletal	confusion, drowsiness,
			muscle. GLUT4 is the primary	nonketotic hyperglycemic-
			insulin-responsive glucose	hyperosmolar coma,
			transporter in fat and muscle	cardiovascular disease (e.g.,
			tissue. Exemplary assays that	heart disease, atherosclerosis,
			may be used or routinely	microvascular disease,
			modified to test for DMEF1	hypertension, stroke, and other
			response element activity (in	diseases and disorders as
			adipocytes and pre-adipocytes)	described in the
			by polypeptides of the	"Cardiovascular Disorders"

invention (including antibodies	section below), dyslipidemia,
and agonists or antagonists of	endocrine disorders (as
the invention) include assays	described in the "Endocrine
disclosed in Thai, M.V., et al., J	Disorders" section below),
 Biol Chem, 273(23):14285-92	neuropathy, vision impairment
(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
Chem, 275(21):16323-8	blindness), ulcers and impaired
(2000); Liu, M.L., et al., J Biol	wound healing, and infection
 Chem, 269(45):28514-21	(e.g., infectious diseases and
(1994); "Identification of a 30-	disorders as described in the
base pair regulatory element	"Infectious Diseases" section
and novel DNA binding	below, especially of the
 protein that regulates the	urinary tract and skin). An
 human GLUT4 promoter in	additional highly preferred
transgenic mice", J Biol Chem.	indication is obesity and/or
 2000 Aug 4;275(31):23666-73;	complications associated with
Berger, et al., Gene 66:1-10	obesity. Additional highly
(1988); and, Cullen, B., et al.,	preferred indications include
 Methods in Enzymol.	weight loss or alternatively,
216:362–368 (1992), the	weight gain. Additional highly
contents of each of which is	preferred indications are
 herein incorporated by	complications associated with
reference in its entirety.	insulin resistance.
Adipocytes and pre-adipocytes	
that may be used according to	
these assays are publicly	
available (e.g., through the	
 ATCC) and/or may be	
routinely generated.	
Exemplary cells that may be	
used according to these assays	

	Highly preferred indications include allergy, asthma, and	rhinitis. Additional preferred indications include infections	(e.g., an infectious disease as	described below under	"Infectious Disease"), and	inflammation and	Inflammatory disorders. Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described
include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	This reporter assay measures activation of the NFAT	signaling pathway in HMC-1	Activation of NFAT in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription through the Nuclear Factor of	Activated T cells (NFAT)	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and
	Activation of transcription	through NFAT response element in	immune cells (such	as mast cells).													
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)W	modulate expression of genes	helow) and
	<u>.ii</u>	involved in	immunodeficiencies (e.g., as
	<u></u>	immunomodulatory functions.	described below). Preferred
`	<u>~</u>	Exemplary assays for	indications include neoplastic
*	tra	transcription through the	diseases (e.g., leukemia,
	<u>Z</u>	NFAT response element that	lymphoma, melanoma,
	- m	may be used or routinely	prostate, breast, lung, colon,
	- W	modified to test NFAT-	pancreatic, esophageal,
	ree	response element activity of	stomach, brain, liver, and
	od	polypeptides of the invention	urinary tract cancers and/or as
		(including antibodies and	described below under
	ag	agonists or antagonists of the	"Hyperproliferative
	ui.	invention) include assays	Disorders"). Other preferred
	die	disclosed in Berger et al., Gene	indications include benign
	99	66:1-10 (1998); Cullen and	dysproliferative disorders and
	M	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	21	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85	85:6342-6346 (1988); De Boer	Preferred indications include
	et	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et	et al., J Immunol	leukemias, Hodgkin's disease,
	16	165(12):7215-7223 (2000);	acute lymphocytic anemia
	<u>H</u>	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	la	al., J Exp Med 188:527-537	granulomatous disease,
	1)	(1998), the contents of each of	inflammatory bowel disease,
	[M	which are herein incorporated	sepsis, neutropenia,
	- P	by reference in its entirety.	neutrophilia, psoriasis,
	M	Mast cells that may be used	suppression of immune

reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	
according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of
	Proliferation of preadipose cells (such as 3T3-L1 cells)
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SEAP in 293/ISRE Activation of transcription through cAMP response element (CRE) in pre-adipocytes.	ure based on ATP als the olically	se cell line. It strain of ation. Cells to an selection of See Green Set See Green is herein its	vation of A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease
795	viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically	active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) regulate CREB transcription factors, and modulate expression of genes involved
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nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below)	diabetic neuropathy, nerve disease and nerve damage	(e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and
functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP	signaling pathway. CREB plays a major role in	adipogenesis, and is involved in differentiation into	adipocytes. CRE contains the binding sequence for the	transcription factor CREB	(CRE binding protein).	transcription through the	cAMP response element that	may be used or routinely	modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch	et al., Mol Cell Biol	20(3):1008-1020 (2000); and	Klemm et al., J Biol Chem
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Disorders"), and infection	(c.g., all illections disease as	"Infectious Disease"), Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-peoplastic
modulate growth and other cell functions Exemplary assays	functions. Exemplary assays	AP1 response element that	may be used or routinely	modified to test AP1-response	element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1988); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Rellahan et al., J Biol Chem	272(49):30806-30811 (1997);	Chang et al., Mol Cell Biol	18(9):4986-4993 (1998); and	Fraser et al., Eur J Immunol	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that
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			may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
HSAWZ41	795	Activation of transcription through NFKB response element in immune cells (such as EOL1 cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes.	Highly preferred indications include asthma, allergy, hypersensitivity reactions, and inflammation. Preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), immunological disorders, inflammation and inflammation and as described below under "Immune Activity", and

for "Blood-Related Disorders").				<u> </u>					assays	er et al., Gene	ullen and	1 Enzymol	2); Henthorn	cad Sci USA	88); Valle	munology	(97);	J Exp Med	95); and	1:838-844	ts of each of	ncorporated	entirety.	oorter assay	ncreases in	sible from a	element in	link the	a repeorter	
Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	For example, a reporter assay	(which measures increases in	transcription inducible from a	NFkB responsive element in	EOL-1 cells) may link the	NFKB element to a repeorter	•
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		Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammaton and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders"), and/or "Cardiovascular Disorders").
transcription factor, which is upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important in the allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Eol-1 is a human eosinophil cell line.		This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including
	SEAP in HIB/CRE	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
	795	795
	HSAWZ41	HSAWZ41

24 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -		Common to disortions in all and
antibodies and agonists of		Freierred indications include
antagonists of the invention) to		autoimmune diseases (e.g.,
regulate GATA3 transcription		rheumatoid arthritis, systemic
factors and modulate	dnl	lupus erythematosis, multiple
 expression of mast cell genes		sclerosis and/or as described
important for immune response		below) and
development. Exemplary		immunodeficiencies (e.g., as
assays for transcription		described below). Preferred
through the GATA3 response		indications include neoplastic
element that may be used or		diseases (e.g., leukemia,
routinely modified to test		lymphoma, melanoma,
 GATA3-response element		prostate, breast, lung, colon,
activity of polypeptides of the		pancreatic, esophageal,
invention (including antibodies		stomach, brain, liver, and
and agonists or antagonists of		urinary tract cancers and/or as
the invention) include assays		described below under
disclosed in Berger et al., Gene		"Hyperproliferative
66:1-10 (1998); Cullen and		Disorders"). Other preferred
Malm, Methods in Enzymol		indications include benign
216:362-368 (1992); Henthorn		dysproliferative disorders and
et al., Proc Natl Acad Sci USA		pre-neoplastic conditions, such
85:6342-6346 (1988); Flavell		as, for example, hyperplasia,
et al., Cold Spring Harb Symp		metaplasia, and/or dysplasia.
Quant Biol 64:563-571 (1999);		Preferred indications include
Rodriguez-Palmero et al., Eur		anemia, pancytopenia,
 J Immunol 29(12):3914-3924		leukopenia, thrombocytopenia,
(1999); Zheng and Flavell,	-	leukemias, Hodgkin's disease,
Cell 89(4):587-596 (1997); and		acute lymphocytic anemia
Henderson et al., Mol Cell Biol		(ALL), plasmacytomas,
14(6):4286-4294 (1994), the		multiple myeloma, Burkitt's
contents of each of which are		lymphoma, arthritis, AIDS,

				herein incorporated by reference in its entirety. Mast cells that may be used	granulomatous disease, inflammatory bowel disease, sepsis, neutropenia,
				according to these assays are publicly available (e.g., through the ATCC).	suppression of immune reactions to transplanted
				Exemplary human mast cells that may be used according to	organs and tissues, hemophilia,
-				these assays include the HMC-	mellitus, endocarditis,
				l cell line, which is an	meningitis, and Lyme Disease.
				innmature numan mast cell line established from the peripheral	
				blood of a patient with mast	
		-		cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HSAWZ41	795	Activation of	This reporter assay measures	Highly preferred indications
			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").

		,	al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of	granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
HSAWZ41	795	Activation of transcription through serum response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune

	cell line with cytolytic and	leukemia, lymphoma,
	evtotoxic activity.	melanoma glioma (e.g.
		malignant glioma). solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
-		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues, hemophilia,
		hypercoagulation, diabetes
		mellitus, endocarditis,
		meningitis, Lyme Disease,
		cardiac reperfusion injury, and

				asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HSAWZ41	795	SEAP in OE-21		
HSAWZ41	795	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include neoplastic diseases
		through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
		response element in	Site (GAS) response element	and/or as described below
		immune cells (such	are well-known in the art and	under "Hyperproliferative
		as T-cells).	may be used or routinely	Disorders"). Highly preferred
			modified to assess the ability	indications include neoplasms
			of polypeptides of the	and cancers, such as, for
			invention (including antibodies	example, leukemia, lymphoma
			and agonists or antagonists of	(e.g., T cell lymphoma,
			the invention) to regulate	Burkitt's lymphoma, non-
			STAT transcription factors and	Hodgkins lymphoma,
			modulate gene expression	Hodgkin"s disease),
-			involved in a wide variety of	melanoma, and prostate,
			cell functions. Exemplary	breast, lung, colon, pancreatic,
	-		assays for transcription	esophageal, stomach, brain,
			through the GAS response	liver and urinary cancer. Other
			element that may be used or	preferred indications include
			routinely modified to test	benign dysproliferative
			GAS-response element activity	disorders and pre-neoplastic
			of polypeptides of the	conditions, such as, for
			invention (including antibodies	example, hyperplasia,
			and agonists or antagonists of	metaplasia, and/or dysplasia.
			the invention) include assays	Preferred indications include
			disclosed in Berger et al., Gene	autoimmune diseases (e.g.,

rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia
66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).														
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leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred inflammation and inflammation and inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g.,
	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription
	Activation of transcription through STAT6 response element in immune cells (such as T-cells).
	795
	HSAWZ41

	through the STAT6 response	rheumatoid arthritis, systemic
	element that may be used or	lupus erythematosis, multiple
	routinely modified to test	sclerosis and/or as described
	STAT6 response element	below) and
_	activity of the polypeptides of	immunodeficiencies (e.g., as
	the invention (including	described below).
	antibodies and agonists or	Preferred indications include
	antagonists of the invention)	neoplastic diseases (e.g.,
	include assays disclosed in	leukemia, lymphoma,
	Berger et al., Gene 66:1-10	melanoma, and/or as described
-	(1998); Cullen and Malm,	below under
	Methods in Enzymol 216:362-	"Hyperproliferative
	368 (1992); Henthorn et al.,	Disorders"). Preferred
	Proc Natl Acad Sci USA	indications include neoplasms
	85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
-	et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
	(1998); Moffatt et al.,	prostate, breast, lung, colon,
	Transplantation 69(7):1521-	pancreatic, esophageal,
	1523 (2000); Curiel et al., Eur	stomach, brain, liver and
	J Immunol 27(8):1982-1987	urinary cancer. Other preferred
	(1997); and Masuda et al., J	indications include benign
	Biol Chem 275(38):29331-	dysproliferative disorders and
	29337 (2000), the contents of	pre-neoplastic conditions, such
	each of which are herein	as, for example, hyperplasia,
	incorporated by reference in its	metaplasia, and/or dysplasia.
	entirety. T cells that may be	Preferred indications include
	used according to these assays	anemia, pancytopenia,
	are publicly available (e.g.,	leukopenia, thrombocytopenia,
	through the ATCC).	Hodgkin's disease, acute
	Exemplary T cells that may be	lymphocytic anemia (ALL),
	used according to these assays	plasmacytomas, multiple

			include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infectious desease as described below under "Infectious
HSAXA83	962	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or

"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis.	systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described	below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional	highly preferred indications include inflammation and	inflammatory disorders, and treating joint damage in	patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.	Highly preferred indications include neoplastic diseases	and/or as described below under "Hyperproliferative Disorders") Additionally	highly preferred indications include neoplasms and	cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g.,
SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) include assays disclosed in	Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992): Henthorn et al	Proc Natl Acad Sci USA 85:6342-6346 (1988); and	Black et al., Virus Genes 12(2):105-117 (1997), the	content of each of which are herein incorporated by	reference in its entirety. T cells that may be used according to these assays are	publicly available (e.g., through the ATCC).	may be used according to these assays include the CTLL cell line which is an II?	dependent suspension culture of T cells with cytotoxic	activity.

is infection (e.g., an infectious disease as described below under "Infectious Disease").	Endothelial Cell Caspase Apoptosis. Assays for	known in the art and may be includes a method for	used or routinely modified to stimulating endothelial cell	assess the ability of growth. An alternative highly	nvention	(including antibodies and invention includes a method	the	 protease-mediated apoptosis. embodiment of the invention	Induction of apoptosis in includes a method for	endothelial cells supporting the stimulating endothelial cell	 associated with tumor highly preferred embodiment	regression due to loss of tumor of the invention includes a	blood supply. Exemplary method for inhibiting	assays for caspase apoptosis endothelial cell proliferation.	that may be used or routinely A highly preferred	modified to test capase embodiment of the invention	apoptosis activity of includes a method for	polypeptides of the invention stimulating apoptosis of	(including antibodies and endothelial cells. An	agonists or antagonists of the alternative highly preferred	invention) include the assays embodiment of the invention	disclosed in Lee et al., FEBS includes a method for	Lett 485(2-3): 122-126 (2000); inhibiting (e.g., decreasing)	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
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embodiment of the invention includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial
and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.										
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infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	
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angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as
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as	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.
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798 Activation of transcription through serum response element in immune cells (such as T-cells).	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include	n a n. n. a n. n. de n. de n. a	ivation of A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative peptides of invention includes a method for stimulating (e.g., increasing) TNF alpha
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	antagonists of the invention) to	production. Preferred
	regulate the serum response	indications include blood
	factors and modulate the	disorders (e.g., as described
	expression of genes involved	below under "Immune
	in growth. Exemplary assays	Activity", "Blood-Related
-	for transcription through the	Disorders", and/or
	SRE that may be used or	"Cardiovascular Disorders"),
	routinely modified to test SRE	Highly preferred indications
	activity of the polypeptides of	include autoimmune diseases
-	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
	antagonists of the invention)	Crohn"s disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
	cells that may be used	arthritis. An additional highly
	according to these assays are	preferred indication is sepsis.
_	publicly available (e.g.,	Highly preferred indications
	through the ATCC).	include neoplastic diseases
····	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be used according to these	and/or as described below
	assays include the CTLL cell	under "Hyperproliferative

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dditional	d indicati	sms and	is, for exa	ohoma,	oma (e.g.,	ma), solic	ostate, bre	ncreatic,	mach, bi	ry cancer.	ations inc	iferative	re-neople	h as, for	rplasia,	I/or dyspl	ations inc	openia,	ombocyte	ase, acute	nemia (AI	s, multiple	citt's lym _l	, granulor	matory be	penia,	soriasis,	immune	nsplanted	
Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	• •
Disc	high	inch	canc	leuk	mela	mali	tume	lung	esob	liver	pref	beni	diso	cond	exau	meta	Pref	anen	leuk	Hod	lyml	plası	mye	arthr	dise	dise	neut	ddns	react	
line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.																											_
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-				hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HSDEK49	798	Regulation of transcription of Malic Enzyme in adipocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesisand its expression is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,
			Exemplary assays that may be	nonketotic hyperglycemic-

	used or routinely modified to	hyperosmolar coma.
	test for regulation of	cardiovascular disease (e.g.,
	transcription of Malic Enzyme	heart disease, atherosclerosis,
	(in adipoocytes) by	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in: Streeper, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	Disorders" section below),
	Endocrinol, 8(10):1361-9	neuropathy, vision impairment
	(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
	Biol Chem, 274(25):17997-	blindness), ulcers and impaired
	8004 (1999); Ijpenberg, A., et	wound healing, and infection
	al., J Biol Chem,	(e.g., infectious diseases and
-	272(32):20108-20117 (1997);	disorders as described in the
	Berger, et al., Gene 66:1-10	"Infectious Diseases" section
	(1988); and, Cullen, B., et al.,	below, especially of the
	Methods in Enzymol.	urinary tract and skin), carpal
	216:362–368 (1992), the	tunnel syndrome and
	contents of each of which is	Dupuytren's contracture).
	herein incorporated by	An additional highly preferred
	reference in its entirety.	indication is obesity and/or
	Hepatocytes that may be used	complications associated with
	according to these assays are	obesity. Additional highly
	publicly available (e.g.,	preferred indications include
	through the ATCC) and/or	weight loss or alternatively,
	may be routinely generated.	weight gain. Aditional
	Exemplary hepatocytes that	highly preferred indications are

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complications associated with insulin resistance.		A highly preferred	indication is diabetes mellitus.	An additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other
may be used according to these assays includes the H4IIE rat liver hepatoma cell line.		Assays for the regulation of	transcription through the	PEPCK promoter are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to activate the	PEPCK promoter in a reporter	construct and regulate liver	gluconeogenesis. Exemplary	assays for regulation of	transcription through the	PEPCK promoter that may be	used or routinely modified to	test for PEPCK promoter	activity (in hepatocytes) of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn
	MIP-1a in HMC	Regulation of	transcription	through the PEPCK	promoter in	hepatocytes																						
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	HSDEK49	HSDFJ26																										

ci USA diseases and disorders as described in the "Cardiovascular Disorders"			>	ay be	assays wound healing, infection (e.g.,		ated. "Infectious Diseases" section		urinary tract and skin), carpal	ys tunnel syndrome and	<u> </u>				obesity. Additional highly	preferred indications include	r alten	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems
et al., Proc Natl Acad Sci USA 85:6342-6346 (1988);	49(6):896-903 (2000); and Yeagley et al., J Biol Chem	275(23):17814-17820 (2000), the contents of each of which	is herein incorporated by	Hepatocyte cells that may be	used according to these assays	through the ATCC) and/or	may be routinely generated.	Exemplary liver hepatoma	cells that may be used	according to these assays	include H4lle cells, which	contain a tyrosine amino	transferase that is inducible	with glucocorticoids, insulin,	or cAMP derivatives.									

_		including myopathies,
		muscular dystrophy, and/or as
		described herein.
		Additional highly preferred
		indications include glycogen
		storage disease (e.g.,
		glycogenoses), hepatitis,
		gallstones, cirrhosis of the
		liver, degenerative or necrotic
		liver disease, alcoholic liver
		diseases, fibrosis, liver
		regeneration, metabolic
		disease, dyslipidemia and
		cholesterol metabolism, and
		hepatocarcinomas.
		Highly preferred indications
		include blood disorders (e.g.,
		as described below under
		"Immune Activity",
		"Cardiovascular Disorders",
		and/or "Blood-Related
		Disorders"), immune disorders
		(e.g., as described below under
		"Immune Activity"), infection
		(e.g., an infectious disease
		and/or disorder as described
		below under "Infectious
		Disease"), endocrine disorders
		(e.g., as described below under
		"Endocrine Disorders"), and
		neural disorders (e.g. as

			described below under "Neural
			Activity and incurvingstrat Diseases").
			Additional preferred
			indications include neoplastic
			diseases (e.g., as described
			"Hyperproliferative
			Disorders"). Preferred
			indications include neoplasms
			and cancers, such as, leukemia,
			lymphoma, prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			and urinary cancer. A highly
			preferred indication is liver
			cancer. Other preferred
			indications include benign
			dysproliferative disorders and
			pre-neoplastic conditions, such
			as, for example, hyperplasia,
			metaplasia, and/or dysplasia.
008	Protection from	Caspase Apoptosis Rescue.	A highly preferred
	Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
7	Apoptosis.	rescue are well known in the	includes a method for
		art and may be used or	stimulating endothelial cell
		routinely modified to assess	growth. An alternative highly
		the ability of the polypeptides	preferred embodiment of the
		of the invention (including	invention includes a method
		antibodies and agonists or	for inhibiting endothelial cell
		antagonists of the invention) to	growth. A highly preferred

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embodiment of the invention	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	growth. An alternative highly	preferred embodiment of the	invention includes a method	for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred
inhihit caspase protease-	mediated apoptosis.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	caspase apoptosis rescue of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Romeo et al.,	Cardiovasc Res 45(3): 788-794	(2000); Messmer et al., Br J	Pharmacol 127(7): 1633-1640	(1999); and J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but
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embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for reducing cardiac	hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include	neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of	the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis,	cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular	disease, diabetic nephropauny, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders").
are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.					

Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary
hemangioendothelioma, angiosarcoma, haemangiopericytoma,

lymphangioma.	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as
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wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related
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				Disorders", and/or
				"Cardiovascular Disorders").
-				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
				described below). Additional
-		•		preferred indications include
				inflammation and
				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HSDJJ82	800	IL-6 in HUVEC		
HSDSB09	801	SEAP in 293/ISRE		
HSDSB09	801	Regulation of	Assays for the regulation of	A highly preferred indication
		transcription via	transcription through the	is diabetes mellitus.
		DMEF1 response	DMEF1 response element are	Additional highly preferred
		element in	well-known in the art and may	indications include
		adipocytes and pre-	be used or routinely modified	complications associated with
		adipocytes	to assess the ability of	diabetes (e.g., diabetic
			polypeptides of the invention	retinopathy, diabetic
			(including antibodies and	nephropathy, kidney disease
			agonists or antagonists of the	(e.g., renal failure,
			invention) to activate the	nephropathy and/or other
			DMEF1 response element in a	diseases and disorders as

renorter construct (such as that	described in the "Renal
containing the GLUT4	Disorders" section below).
nromoter) and to regulate	diabetic neuronathy nerve
 insulin production. The	disease and nerve damage
 DMEF1 response element is	(e.g., due to diabetic
present in the GLUT4	neuropathy), blood vessel
promoter and binds to MEF2	blockage, heart disease, stroke,
 transcription factor and another	impotence (e.g., due to diabetic
transcription factor that is	neuropathy or blood vessel
required for insulin regulation	blockage), seizures, mental
of Glut4 expression in skeletal	confusion, drowsiness,
muscle. GLUT4 is the primary	nonketotic hyperglycemic-
insulin-responsive glucose	hyperosmolar coma,
transporter in fat and muscle	cardiovascular disease (e.g.,
tissue. Exemplary assays that	heart disease, atherosclerosis,
may be used or routinely	microvascular disease,
modified to test for DMEF1	hypertension, stroke, and other
response element activity (in	diseases and disorders as
adipocytes and pre-adipocytes)	described in the
 by polypeptides of the	"Cardiovascular Disorders"
invention (including antibodies	section below), dyslipidemia,
and agonists or antagonists of	endocrine disorders (as
the invention) include assays	described in the "Endocrine
disclosed in Thai, M.V., et al., J	Disorders" section below),
Biol Chem, 273(23):14285-92	neuropathy, vision impairment
 (1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
Chem, 275(21):16323-8	blindness), ulcers and impaired
(2000); Liu, M.L., et al., J Biol	wound healing, and infection
Chem, 269(45):28514-21	(e.g., infectious diseases and
(1994); "Identification of a 30-	disorders as described in the
base pair regulatory element	"Infectious Diseases" section

		DNIA Linding	holow amanially of the	_
		and novel DivA binding	using tract and chin) An	
		protein that regulates the	urinary tract and skin). An	
		human GLUT4 promoter in	additional highly preferred	
		transgenic mice", J Biol Chem.	indication is obesity and/or	-
		2000 Aug 4;275(31):23666-73;	complications associated with	_
		Berger, et al., Gene 66:1-10	obesity. Additional highly	
		(1988); and, Cullen, B., et al.,	preferred indications include	
		Methods in Enzymol.	weight loss or alternatively,	
		216:362–368 (1992), the	weight gain. Additional highly	
		contents of each of which is	preferred indications are	
		herein incorporated by	complications associated with	
		reference in its entirety.	insulin resistance.	
		Adipocytes and pre-adipocytes		
		that may be used according to		
		these assays are publicly		
		available (e.g., through the		
-		ATCC) and/or may be		
		routinely generated.		
		Exemplary cells that may be		
		used according to these assays		
		include the mouse 3T3-L1 cell		
		line which is an adherent		
		mouse preadipocyte cell line.		
		Mouse 3T3-L1 cells are a		
		continuous substrain of 3T3		
		fibroblasts developed through		
		clonal isolation. These cells		
		undergo a pre-adipocyte to		
		adipose-like conversion under		
		appropriate differentiation		
		culture conditions.		

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A highly preferred indication is obesity and/or complications	associated with obesity.	Additional highly preferred	indications include weight loss	or alternatively, weight gain.	An additional highly preferred	indication is diabetes mellitus.	An additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease atheroscilerosis
Assays for the activation of transcription through the	cAMP response element are	well-known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to increase cAMP,	regulate CREB transcription	factors, and modulate	expression of genes involved	in a wide variety of cell	functions. For example, a	3T3-L1/CRE reporter assay	may be used to identify factors	that activate the cAMP	signaling pathway. CREB	plays a major role in	adipogenesis, and is involved	in differentiation into	adipocytes. CRE contains the	binding sequence for the	transcription factor CREB	(CRE binding protein).	Exemplary assays for	transcription through the	cAMP response element that	may be used or routinely	modified to test cAMP.
Activation of transcription	through cAMP	response element	(CRE) in pre-	adipocytes.	•																								
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	response element activity of	microvascular disease.
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in Berger et al., Gene	section below), dyslipidemia,
·	66:1-10 (1998); Cullen and	endocrine disorders (as
	 Malm, Methods in Enzymol	described in the "Endocrine
	216:362-368 (1992); Henthorn	Disorders" section below),
	et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
	85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
	 et al., Mol Cell Biol	blindness), ulcers and impaired
	20(3):1008-1020 (2000); and	wound healing, and infection
	Klemm et al., J Biol Chem	(e.g., infectious diseases and
	 273:917-923 (1998), the	disorders as described in the
	contents of each of which are	"Infectious Diseases" section
	herein incorporated by	below, especially of the
	reference in its entirety. Pre-	urinary tract and skin), carpal
	adipocytes that may be used	tunnel syndrome and
	according to these assays are	Dupuytren's contracture).
	publicly available (e.g.,	Additional highly preferred
	through the ATCC) and/or	indications are complications
	may be routinely generated.	associated with insulin
	Exemplary mouse adipocyte	resistance.
	 cells that may be used	
	according to these assays	
	include 3T3-L1 cells. 3T3-L1	
	is an adherent mouse	
	 preadipocyte cell line that is a	
	continuous substrain of 3T3	
	fibroblast cells developed	

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·	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental
through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al.,
	Activation of transcription through serum response element in pre-adipocytes.
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				Proc Natl Acad Sci USA	confusion, drowsiness,
				85:6342-6346 (1988); and	nonketotic hyperglycemic-
				Black et al., Virus Genes	hyperosmolar coma,
				12(2):105-117 (1997), the	cardiovascular disease (e.g.,
				content of each of which are	heart disease, atherosclerosis,
				herein incorporated by	microvascular disease,
				reference in its entirety. Pre-	hypertension, stroke, and other
				adipocytes that may be used	diseases and disorders as
				according to these assays are	described in the
				publicly available (e.g.,	"Cardiovascular Disorders"
				through the ATCC) and/or	section below), dyslipidemia,
				may be routinely generated.	endocrine disorders (as
				Exemplary mouse adipocyte	described in the "Endocrine
_				cells that may be used	Disorders" section below),
_				according to these assays	neuropathy, vision impairment
				include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
				is an adherent mouse	blindness), ulcers and impaired
				preadipocyte cell line that is a	wound healing, and infection
				continuous substrain of 3T3	(e.g., infectious diseases and
				fibroblast cells developed	disorders as described in the
				through clonal isolation and	"Infectious Diseases" section
				undergo a pre-adipocyte to	below). Additional highly
				adipose-like conversion under	preferred indications are
				appropriate differentiation	complications associated with
				conditions known in the art.	insulin resistance.
	HSDSB09	801	SEAP in Alk Phos C2C12		
	HSDSB09	801	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha

	immune cells (such	art and may be used or	production. An alternative
	as T-cells).	routinely modified to assess	preferred embodiment of the
		the ability of polypeptides of	invention includes a method
		the invention (including	for stimulating (e.g.,
		antibodies and agonists or	increasing) TNF alpha
		antagonists of the invention) to	production. Preferred
		regulate the serum response	indications include blood
		factors and modulate the	disorders (e.g., as described
		expression of genes involved	below under "Immune
		in growth. Exemplary assays	Activity", "Blood-Related
		for transcription through the	Disorders", and/or
		SRE that may be used or	"Cardiovascular Disorders"),
		routinely modified to test SRE	Highly preferred indications
		activity of the polypeptides of	include autoimmune diseases
		the invention (including	(e.g., rheumatoid arthritis,
		antibodies and agonists or	systemic lupus erythematosis,
		antagonists of the invention)	Crohn"s disease, multiple
 -		include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and	immune response. Additional
		Black et al., Virus Genes	highly preferred indications
		12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
		herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
		cells that may be used	arthritis. An additional highly
		according to these assays are	preferred indication is sepsis.

Highly preferred indications include neoplastic diseases t (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally.		malignant glioma, v.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel
publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line which is an II -2	dependent suspension culture of T cells with cytotoxic activity.			
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disea neutr supp react organ hemo diabo meni cardi asthr addii is ini disea unde	Sulation of A highly preferred indication is diabetes mellitus. An additional highly preferred outinely associated with diabetes (e.g., diabetic retinopathy, diabetic diabetic retinopathy and/or other nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), ts expression is two direct (e.g., due to diabetic neuropathy), blood vessel dentified as highlic Enzyme, disease and nerve damage and the collabetic neuropathy), blood vessel dentified as highlic browns in the collabetic neuropathy), blood vessel dentified as highlic browns in the collabetic neuropathy), blood vessel dentified as highlic browns in the collabetic neuropathy), blood vessel
	of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesisand its expression is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements
	ranscription of Malic Enzyme in adipocytes
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		nutative PPAR response	impotence (e.g., due to diabetic
		 pummer in the momentum more	namenathy or blood yessel
		elements. Ivie promoter may	nemopanily of oloon vesser
		also responds to AP1 and other	blockage), seizures, mental
		transcription factors.	confusion, drowsiness,
		Exemplary assays that may be	nonketotic hyperglycemic-
		used or routinely modified to	hyperosmolar coma,
		test for regulation of	cardiovascular disease (e.g.,
	_	transcription of Malic Enzyme	heart disease, atherosclerosis,
		(in adipoocytes) by	microvascular disease,
		polypeptides of the invention	hypertension, stroke, and other
		(including antibodies and	diseases and disorders as
	-	agonists or antagonists of the	described in the
		invention) include assays	"Cardiovascular Disorders"
		disclosed in: Streeper, R.S., et	section below), dyslipidemia,
		al., Mol Endocrinol,	endocrine disorders (as
		12(11):1778-91 (1998);	described in the "Endocrine
		Garcia-Jimenez, C., et al., Mol	Disorders" section below),
_		Endocrinol, 8(10):1361-9	neuropathy, vision impairment
		(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
		Biol Chem, 274(25):17997-	blindness), ulcers and impaired
		8004 (1999); Ijpenberg, A., et	wound healing, and infection
		al., J Biol Chem,	(e.g., infectious diseases and
		272(32):20108-20117 (1997);	disorders as described in the
		 Berger, et al., Gene 66:1-10	"Infectious Diseases" section
		(1988); and, Cullen, B., et al.,	below, especially of the
		Methods in Enzymol.	urinary tract and skin), carpal
		216:362–368 (1992), the	tunnel syndrome and
		 contents of each of which is	Dupuytren's contracture).
		herein incorporated by	An additional highly preferred
		reference in its entirety.	indication is obesity and/or
	:	Hepatocytes that may be used	complications associated with

			according to these assays are publicly available (e.g., through the ATCC) and/or	obesity. Additional highly preferred indications include weight loss or alternatively,
			may be routinely generated.	weight gain. Aditional
			Exemplary hepatocytes that	highly preferred indications are
			may be used according to these	complications associated with
			assays includes the H4IIE rat	insulin resistance.
			liver hepatoma cell line.	
HSDSB09	801	SEAP in HIB/CRE		
60BSGSH	801	Stimulation of	Assays for measuring calcium	A highly preferred
		Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
		pancreatic beta	and may be used or routinely	An additional highly preferred
		cells.	modified to assess the ability	indication is a complication
			of polypeptides of the	associated with diabetes (e.g.,
			invention (including antibodies	diabetic retinopathy, diabetic
			and agonists or antagonists of	nephropathy, kidney disease
			the invention) to mobilize	(e.g., renal failure,
			calcium. For example, the	nephropathy and/or other
			FLPR assay may be used to	diseases and disorders as
			measure influx of calcium.	described in the "Renal
			Cells normally have very low	Disorders" section below),
			concentrations of cytosolic	diabetic neuropathy, nerve
			calcium compared to much	disease and nerve damage
			higher extracellular calcium.	(e.g., due to diabetic
			Extracellular factors can cause	neuropathy), blood vessel
			an influx of calcium, leading to	blockage, heart disease, stroke,
			activation of calcium	impotence (e.g., due to diabetic
			responsive signaling pathways	neuropathy or blood vessel
			and alterations in cell	blockage), seizures, mental
			functions. Exemplary assays	confusion, drowsiness,
			that may be used or routinely	nonketotic hyperglycemic-

hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below),	neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired	wound healing, and infection (e.g., infectious diseases and disorders as described in the	"Intectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and		obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are
modified to measure calcium flux by polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) include assays disclosed in: Satin LS, et al., Endocrinology, 136(10):4589-601 (1995);Mogami H, et al.,	Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al.,	Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is	herein incorporated by reference in its entirety. Pancreatic cells that may be	used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated.	Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent	epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and

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complications associated with insulin resistance.			Highly preferred indications	include allergy, asthma, and	indications include infection	(e.g., an infectious disease as	described below under	"Infectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described
glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and	glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and	Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78:	This reporter assay measures	activation of the GATA-3	signaling pathway in FIMC-1 human mast cell line.	Activation of GATA-3 in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the GATA3 response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate GATA3 transcription	factors and modulate	expression of mast cell genes
			Activation of	transcription	through GAIA-3 response element in	immune cells (such	as mast cells).	`													
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below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	Iymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune
important for immune response	development. Exemplary	assays for transcription	through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,
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			through the ATCC). Exemplary human mast cells that may be used according to	reactions to transplanted organs and tissues, hemophilia, hymercoamilation diabetes
			these assays include the HMC-	mellitus, endocarditis,
			1 cell line, which is an	meningitis, and Lyme Disease.
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HSDSB09	801	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the NFAT	include allergy, asthma, and
		through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and
	<u>.</u>		activation of transcription	inflammatory disorders.
			through the Nuclear Factor of	Preferred indications also
			Activated T cells (NFAT)	include blood disorders (e.g.,
			response element are well-	as described below under
			known in the art and may be	"Immune Activity", "Blood-
			used or routinely modified to	Related Disorders", and/or
			assess the ability of	"Cardiovascular Disorders").
			polypeptides of the invention	Preferred indications include
			(including antibodies and	autoimmune diseases (e.g.,
			agonists or antagonists of the	rheumatoid arthritis, systemic
			invention) to regulate NFAT	lupus erythematosis, multiple
	!		transcription factors and	sclerosis and/or as described

	modulate expression of genes	below) and
	involved in	immunodeficiencies (e.g., as
	immunomodulatory functions.	described below). Preferred
	Exemplary assays for	indications include neoplastic
	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
	may be used or routinely	prostate, breast, lung, colon,
	modified to test NFAT-	pancreatic, esophageal,
	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
-	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,
	which are herein incorporated	sepsis, neutropenia,
	by reference in its entirety.	neutrophilia, psoriasis,
	Mast cells that may be used	suppression of immune

transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for immunodeficiencies (e.g., as transcription through the may be used or rountinely modified to test NFKB-modified to test note note to test	υ πα ∞ ν
transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Stassen et al., J Immunol 166(7):4391-8 (2001); and Marquardt and Walker, J Allergy Clin Immunol 105(3):500-5 (2000), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).	transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1988); Stassen et al., J Immunol 166(7):4391-8 (2001); and Marquardt and Walker, J Allergy Clin Immunol 105(3):500-5 (2000), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).

	Highly preferred indications include allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include hematopoietic and immunological disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and
that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element in immune cells (such as in the human HMC-1 mast cell line) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element
	Activation of transcription through STAT6 response element in immune cells (such as mast cells).
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	activity of the polypeptides of	described below). Preferred
	the invention (including	indications include neoplastic
	antibodies and agonists or	diseases (e.g., leukemia,
	antagonists of the invention)	lymphoma, melanoma, and/or
	include assays disclosed in	as described below under
	Berger et al., Gene 66:1-10	"Hyperproliferative
	(1998); Cullen and Malm,	Disorders"). Preferred
	Methods in Enzymol 216:362-	indications include neoplasms
	368 (1992); Henthorn et al.,	and cancer, such as, for
	Proc Natl Acad Sci USA	example, leukemia, lymphoma,
	85:6342-6346 (1988);	melanoma, and prostate,
-	Sherman, Immunol Rev	breast, lung, colon, pancreatic,
	179:48-56 (2001); Malaviya	esophageal, stomach, brain,
	and Uckun, J Immunol	liver and urinary cancer. Other
	168:421-426 (2002); Masuda	preferred indications include
	et al., J Biol Chem	benign dysproliferative
	275(38):29331-29337 (2000);	disorders and pre-neoplastic
	and Masuda et al., J Biol Chem	conditions, such as, for
	276:26107-26113 (2001), the	example, hyperplasia,
	contents of each of which are	metaplasia, and/or dysplasia.
	herein incorporated by	Preferred indications include
	reference in its entirety. Mast	hematopoietic and
	cells that may be used	immunological disorders such
	according to these assays are	as arthritis, AIDS,
	publicly available (e.g.,	granulomatous disease,
	through the ATCC).	inflammatory bowel disease,
	Exemplary human mast cells	sepsis, neutropenia,
	that may be used according to	neutrophilia, psoriasis,
	these assays include the HMC-	suppression of immune
	1 cell line, which is an	reactions to transplanted
	immature human mast cell line	organs and tissues, hemophilia,

	٠		These cells retain	highly preferred indications are
			pancreatic beta cells including	compilications associated with insulin resistance.
			glucose inducible insulin	
			secretion. References: Asfari	
			et al. Endocrinology 1992 130:167.	
HSDSB09	801	SEAP in Jurkat/IL4		
		promoter		
HSDSB09	801	SEAP in Jurkat/IL4		
		promoter (antiCD3		
		co-stim)		
HSDSB09	801	Activation of	This reporter assay measures	Highly preferred indication
		transcription	activation of the NFkB	includes allergy, asthma, and
		through NFKB	signaling pathway in Ku812	rhinitis. Additional highly
		response element in	human basophil cell line.	preferred indications include
		immune cells (such	Assays for the activation of	infection (e.g., an infectious
		as basophils).	transcription through the	disease as described below
			NFKB response element are	under "Infectious Disease"),
			well-known in the art and may	and inflammation and
			be used or routinely modified	inflammatory disorders.
			to assess the ability of	Preferred indications include
			polypeptides of the invention	immunological and
			(including antibodies and	hempatopoietic disorders (e.g.,
			agonists or antagonists of the	as described below under
			invention) to regulate NFKB	"Immune Activity", and
			transcription factors and	"Blood-Related Disorders").
			modulate expression of	Preferred indications also
			immunomodulatory genes.	include autoimmune diseases
-			Exemplary assays for	(e.g., rheumatoid arthritis,
			transcription through the	systemic lupus erythematosis.

		-																												
multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative	Disorders".										
NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Basophils that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used	according to these assays	include Ku812, originally	established from a patient with	chronic myelogenous	leukemia. It is an immature	prebasophilic cell line that can
								-																		-				
											-																		_	
						_																			_					

				be induced to differentiate into mature basophils.	
	HSDSB09	801	SEAP in		
			Ku812/NFkB (TNF		
			synergy)		
	HSDSB09	801	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
_			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
104				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
		********		genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and

Malm, Methods in Enzymol 216:362-368 (1992); Henthom 85:632-6346 (1988); Benson 88:73 (1994); and Black et al., Virus General (1997), the content of each of (1997), the content of (1997), the			
Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862- 3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly	preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and	cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of	which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line,	which is a human natural killer cell line with cytolytic and cytotoxic activity.

			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues, hemophilia,
			hypercoagulation, diabetes
	-12		mellitus, endocarditis,
			meningitis, Lyme Disease,
			cardiac reperfusion injury, and
			asthma and allergy. An
			additional preferred indication
			is infection (e.g., an infectious
-			disease as described below
			under "Infectious Disease").
HSDSB09 801	Activation of	Assays for the activation of	A highly preferred
	transcription	transcription through the	indication is allergy.
	through STAT6	Signal Transducers and	Another highly preferred
	response element in	Activators of Transcription	indication is asthma.
	immune cells (such	(STAT6) response element are	Additional highly preferred
	as T-cells).	well-known in the art and may	indications include
		be used or routinely modified	inflammation and
		to assess the ability of	inflammatory disorders.

polypeptides of the invention	Preferred indications include
(including antibodies and	blood disorders (e.g., as
 agonists or antagonists of the	described below under
invention) to regulate STAT6	"Immune Activity", "Blood-
transcription factors and	Related Disorders", and/or
 modulate the expression of	"Cardiovascular Disorders").
 multiple genes. Exemplary	Preferred indications include
assays for transcription	autoimmune diseases (e.g.,
 through the STAT6 response	rheumatoid arthritis, systemic
element that may be used or	lupus erythematosis, multiple
routinely modified to test	sclerosis and/or as described
STAT6 response element	below) and
activity of the polypeptides of	immunodeficiencies (e.g., as
 the invention (including	described below).
 antibodies and agonists or	Preferred indications include
antagonists of the invention)	neoplastic diseases (e.g.,
 include assays disclosed in	leukemia, lymphoma,
 Berger et al., Gene 66:1-10	melanoma, and/or as described
(1998); Cullen and Malm,	below under
Methods in Enzymol 216:362-	- "Hyperproliferative
368 (1992); Henthorn et al.,	Disorders"). Preferred
Proc Natl Acad Sci USA	indications include neoplasms
 85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
 et al., Blood 92(12):4529-4538	8 Iymphoma, melanoma, and
(1998); Moffatt et al.,	prostate, breast, lung, colon,
Transplantation 69(7):1521-	
1523 (2000); Curiel et al., Eur	stomach, brain, liver and
 J Immunol 27(8):1982-1987	urinary cancer. Other preferred
(1997); and Masuda et al., J	indications include benign
Biol Chem 275(38):29331-	dysproliferative disorders and
29337 (2000), the contents of	pre-neoplastic conditions, such

801 CXCR4 in SW480 Myoblast cell proliferation
1010

	antibodies and agonists or	cardiovascular disorders (such
	antagonists of the invention) to	as congestive heart failure.
	stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
	cell proliferation. Exemplary	congenital cardiovascular
	assays for myoblast cell	abnormalities, heart disease,
	proliferation that may be used	cardiac arrest, heart valve
	or routinely modified to test	disease, vascular disease, and
	activity of polypeptides and	also as described below under
	antibodies of the invention	"Cardiovascular Disorders"),
	(including agonists or	stimulating myoblast
	antagonists of the invention)	proliferation, and inhibiting
	include, for example, assays	myoblast proliferation.
	disclosed in: Soeta, C., et al.	
	"Possible role for the c-ski	
	gene in the proliferation of	
	myogenic cells in regenerating	
	skeletal muscles of rats" Dev	
	Growth Differ Apr;43(2):155-	
	64 (2001); Ewton DZ, et al.,	
	"IGF binding proteins-4, -5	
	and -6 may play specialized	
-	roles during L6 myoblast	
	proliferation and	
	differentiation" J Endocrinol	
	Mar;144(3):539-53 (1995);	
	and, Pampusch MS, et	
-	al., "Effect of transforming	
	growth factor beta on	
-	proliferation of L6 and	
	embryonic porcine myogenic	
	cells" J Cell Physiol	

	
	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under
Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large
	Production of IL-6
	803
	HSDSE75

var	variety of cells where the	Related Disorders", and/or
exi exi	expression level is strongly	"Cardiovascular Disorders"),
reg	regulated by cytokines, growth	and infection (e.g., as
fac	factors, and hormones are well	described below under
knc	known in the art and may be	"Infectious Disease"). Highly
asu nee	used or routinely modified to	preferred indications include
ass	assess the ability of	autoimmune diseases (e.g.,
lod	polypeptides of the invention	rheumatoid arthritis, systemic
(inc	(including antibodies and	lupus erythematosis, multiple
ago	agonists or antagonists of the	sclerosis and/or as described
inv	invention) to mediate	below) and
imi	immunomodulation and	immunodeficiencies (e.g., as
difb	differentiation and modulate T	described below). Highly
cell	cell proliferation and function.	preferred indications also
Exe	Exemplary assays that test for	include boosting a B cell-
imi	immunomodulatory proteins	mediated immune response
eva	evaluate the production of	and alternatively suppressing a
cyte	cytokines, such as IL-6, and	B cell-mediated immune
the	the stimulation and	response. Highly preferred
udn	upregulation of T cell	indications include
pro	proliferation and functional	inflammation and
acti	activities. Such assays that	inflammatory
may	may be used or routinely	disorders.Additional highly
оош	modified to test	preferred indications include
umi	immunomodulatory and	asthma and allergy. Highly
diff	diffferentiation activity of	preferred indications include
flod	polypeptides of the invention	neoplastic diseases (e.g.,
(inc	(including antibodies and	myeloma, plasmacytoma,
ago.	agonists or antagonists of the	leukemia, lymphoma,
inversion of the second of the	invention) include assays	melanoma, and/or as described
disc	disclosed in Miraglia et al., J	below under

⊢	193-	204(1999); Rowland et al., Disorders"). Highly preferred	"Lymphocytes: a practical indications include neoplasms	approach" Chapter 6:138-160 and cancers, such as, myeloma,	(2000); and Verhasselt et al., J plasmacytoma, leukemia,	Immunol 158:2919-2925 Iymphoma, melanoma, and	(1997), the contents of each of prostate, breast, lung, colon,		by reference in its entirety. stomach, brain, liver and	Human dendritic cells that may urinary cancer. Other preferred	be used according to these indications include benign	assays may be isolated using dysproliferative disorders and	techniques disclosed herein or pre-neoplastic conditions, such	otherwise known in the art. as, for example, hyperplasia,	Human dendritic cells are metaplasia, and/or dysplasia.	antigen presenting cells in Preferred indications include	suspension culture, which, anemia, pancytopenia,	when activated by antigen leukopenia, thrombocytopenia,	and/or cytokines, initiate and Hodgkin's disease, acute	upregulate T cell proliferation lymphocytic anemia (ALL),	and functional activities. multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	
-	Biomolecula	204(1999); I	"Lymphocyt	approach" C	(2000); and	Immunol 15	(1997), the c	which are he	by reference	Human dend	be used acco	assays may l	techniques d	otherwise kn	Human dend	antigen prese	suspension c	when activat	and/or cytok	upregulate T	and function										

HSDZR57 HSDZR57	803 803	SEAP in Alk Phos C2C12 SEAP in ATP-3T3- L1 Activation of Endothelial Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced	meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred	
			activity of polypeptides of the invention (including antibodies and agonists or antagonists of	embodiment of the invention includes a method for stimulating apoptosis of	

the invention) include the	endothelial cells. An
 assays disclosed in Forrer et	alternative highly preferred
al., Biol Chem 379(8-9):1101-	embodiment of the invention
1110 (1998); Gupta et al., Exp	includes a method for
Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
 (1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
Soc Symp 64:29-48 (1999);	A highly preferred
 Chang and Karin, Nature	embodiment of the invention
410(6824):37-40 (2001); and	includes a method for
Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
the contents of each of which	alternative highly preferred
are herein incorporated by	embodiment of the invention
reference in its entirety.	includes a method for
Endothelial cells that may be	inhibiting (e.g., decreasing) the
used according to these assays	activation of and/or
 are publicly available (e.g.,	inactivating endothelial cells.
through the ATCC).	A highly preferred
 Exemplary endothelial cells	embodiment of the invention
 that may be used according to	includes a method for
these assays include human	stimulating angiogenisis. An
umbilical vein endothelial cells	alternative highly preferred
(HUVEC), which are	embodiment of the invention
endothelial cells which line	includes a method for
venous blood vessels, and are	inhibiting angiogenesis. A
involved in functions that	highly preferred embodiment
include, but are not limited to,	of the invention includes a
angiogenesis, vascular	method for reducing cardiac
permeability, vascular tone,	hypertrophy. An alternative
and immune cell extravasation.	highly preferred embodiment
	of the invention includes a

method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as	"Hyperproliferative Disorders"), and disorders of the cardiovascular system	heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular	dysfunction, atheroscierosis and atheroscierotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g. systemic	disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins

	and/or lymphatics). Highly
	preferred are indications that
	stimulate angiogenesis and/or
	cardiovascularization. Highly
	preferred are indications that
	inhibit angiogenesis and/or
	cardiovascularization.
	Highly preferred indications
	include antiangiogenic activity
	to treat solid tumors,
	leukemias, and Kaposi"s
	sarcoma, and retinal disorders.
	Highly preferred indications
	include neoplasms and cancer,
	such as, Kaposi"s sarcoma,
	hemangioma (capillary and
 	cavernous), glomus tumors,
	telangiectasia, bacillary
 	angiomatosis,
_	hemangioendothelioma,
	angiosarcoma,
 	haemangiopericytoma,
	lymphangioma,
	lymphangiosarcoma. Highly
 _	preferred indications also
	include cancers such as,
 	prostate, breast, lung, colon,
	pancreatic, esophageal,
	stomach, brain, liver, and
	urinary cancer. Preferred
	indications include benign

	_		disproliferative disorders and
_	_		a) spronterance assumers and
 -			pre-neoplastic conditions, such
 			as, for example, hyperplasia,
 			metaplasia, and/or dysplasia.
			Highly preferred indications
_			also include arterial disease,
,			such as, atherosclerosis,
			hypertension, coronary artery
	-		disease, inflammatory
	_		vasculitides, Reynaud"s
			disease and Reynaud"s
			phenomenom, aneurysms,
			restenosis; venous and
			lymphatic disorders such as
			thrombophlebitis,
			lymphangitis, and
-			lymphedema; and other
		-	vascular disorders such as
			peripheral vascular disease,
			and cancer. Highly
 _			preferred indications also
			include trauma such as
			wounds, burns, and injured
			tissue (e.g., vascular injury
			such as, injury resulting from
			balloon angioplasty, and
 			atheroschlerotic lesions),
			implant fixation, scarring,
 			ischemia reperfusion injury,
 			rheumatoid arthritis,
			cerebrovascular disease, renal

diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as
						-																				_				
							-					-																		
						_				_																				

				described below). Additional
				preferred indications include
				inflammation and
				inflammatory disorders (such
-				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HSIDJ81	804	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
			of insulin are well-known in	is diabetes mellitus. An
			the art and may be used or	additional highly preferred
			routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease
			antagonists of the invention) to	(e.g., renal failure,
			stimulate insulin secretion.	nephropathy and/or other
			For example, insulin secretion	diseases and disorders as
			is measured by FMAT using	described in the "Renal
			anti-rat insulin antibodies.	Disorders" section below),
			Insulin secretion from	diabetic neuropathy, nerve
			pancreatic beta cells is	disease and nerve damage
			upregulated by glucose and	(e.g., due to diabetic
			also by certain	neuropathy), blood vessel
			proteins/peptides, and	blockage, heart disease, stroke,
			disregulation is a key	impotence (e.g., due to diabetic
			component in diabetes.	neuropathy or blood vessel
-			Exemplary assays that may be	blockage), seizures, mental
			used or routinely modified to	confusion, drowsiness,
			test for stimulation of insulin	nonketotic hyperglycemic-

	Correction (from non-reation		manamolaroma
	section (mon panera		nyperosinoiai coma,
	cells) by polypeptides of the		cardiovascular disease (e.g.,
	invention (including antibodies		heart disease, atherosclerosis,
_	and agonists or antagonists of		microvascular disease,
	the invention) include assays		hypertension, stroke, and other
	disclosed in: Shimizu, H., et		diseases and disorders as
	al., Endocr J, 47(3):261-9		described in the
	(2000); Salapatek, A.M., et al.,	t al.,	"Cardiovascular Disorders"
	Mol Endocrinol, 13(8):1305-		section below), dyslipidemia,
	17 (1999); Filipsson, K., et al.,		endocrine disorders (as
	Ann N Y Acad Sci, 865:441-4		described in the "Endocrine
	(1998); Olson, L.K., et al., J	<u> </u>	Disorders" section below),
	Biol Chem, 271(28):16544-52		neuropathy, vision impairment
	(1996); and, Miraglia S et. al.,		(e.g., diabetic retinopathy and
	Journal of Biomolecular		blindness), ulcers and impaired
	Screening, 4:193-204 (1999),		wound healing, and infection
	the contents of each of which		(e.g., infectious diseases and
	is herein incorporated by		disorders as described in the
	reference in its entirety.		"Infectious Diseases" section
	Pancreatic cells that may be		below, especially of the
	used according to these assays		urinary tract and skin), carpal
	are publicly available (e.g.,		tunnel syndrome and
	through the ATCC) and/or		Dupuytren's contracture).
	may be routinely generated.		An additional highly preferred
	Exemplary pancreatic cells that		indication is obesity and/or
	may be used according to these		complications associated with
	assays include HITT15 Cells.		obesity. Additional highly
	HITT15 are an adherent		preferred indications include
	epithelial cell line established		weight loss or alternatively,
-	from Syrian hamster islet cells		weight gain. Additional highly
	transformed with SV40. These		preferred indications are

cells express glucagon, somatostatin, and glucocorticoid receptors. T cells secrete insulin, which stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CI 1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Pro Natl. Acad. Sci. USA 78: 4339-4343, 1981. HSIDJ81 804 Activation of Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Pro Natl. Acad. Sci. USA 78: 4339-4343, 1981. HSIDJ81 804 Activation of Assays for the activation of transcription transcription transcription transcription as SKNMC cells). To assess the ability of polypeptides of the invention of modulate expression of meuronal genes. Exemplary assays for transcription through the hinvention to regulate NFKI transcription factors and agonists or antagonists of the invention assays for transcription through the NFKB response element in personal cells. (such in activation factors and agonists or antagonists of the invention assays for transcription factors and modulate expression of neuronal genes. Exemplary assays for transcription through the neuronal genes. Exemplary assays for transcription factors and modulate expression of neuronal genes. Exemplary assays for transcription element in through the NFKB response element in through the NFKB response element in the art and modulate expression of neuronal genes. Exemplary assays for transcription element in through the NFKB response element in through the NFKB response element in the art and through the NFKB response element in the art and through the NFKB response element in the art and through the NFKB response element in the art and through the NFKB response element in the art and through the NFKB response element in the art and through the NFKB response element in the art and through the NFKB response element in the art and the NFKB response element in the art and through the NFKB response element in the art and through the NFKB response element in the art and through the NFKB response element in the art and through through through the NFK	n, complications associated with insulin resistance. ors. The which is and sed by C# CRL- al. Proc. 78:		ion of Preferred embodiments of the invention include using ent are polypeptides of the invention and may (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, vention prevention, and/or treatment of Neurological Diseases and Disorders (e.g. Alzheimer's Disease, Parkinson''s Disease, nd Brain Cancer, Seizures).
804	cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78:		
		TNFa in Hum	Activation of transcription through NFKI response elem neuronal cells as SKNMC of
HSIDJ81 HSIDJ81		804	804
		HSIDJ81	HSIDJ81

routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gill JS, et al., Neurobiol Dis, 7(4):448-461 (2000); Tamatani M, et al., J Biol Chem, 274(13):8531- 8538 (1999); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J	Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Neuronal cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary neuronal cells that may be used according to these assays are publicly available (e.g., through the ATCC).

				assays include the SKNMC neuronal cell line.	
H	HSKDA27	805	MCP-1 in HUVEC		
H	HSKDA27	805	Production of GM-	GM-CSF FMAT. GM-CSF is	A highly preferred
_			CSF	expressed by activated T cells,	embodiment of the invention
				macrophages, endothelial cells,	includes a method for
				and fibroblasts. GM-CSF	stimulating the production of
				regulates differentiation and	GM-CSF. An alternative
				proliferation of granulocytes-	highly preferred embodiment
				macrophage progenitors and	of the invention includes a
				enhances antimicrobial activity	method for inhibiting the
				in neutrophils, monocytes and	production of GM-CSF.
				macrophage. Additionally,	Highly preferred indications
				GM-CSF plays an important	include inflammation and
				role in the differentiation of	inflammatory disorders. An
				dendritic cells and monocytes,	additional highly preferred
				and increases antigen	indication is infection (e.g., as
_				presentation. GM-CSF is	described below under
				considered to be a	"Infectious Disease".
				proinflammatory cytokine.	Highly preferred indications
				Assays for immunomodulatory	include blood disorders (e.g.,
				proteins that promote the	neutropenia (and the
				production of GM-CSF are	prevention of neutropenia
				well known in the art and may	(e.g., in HIV infected patients),
				be used or routinely modified	and/or as described below
				to assess the ability of	under "Immune Activity",
			-	polypeptides of the invention	"Blood-Related Disorders",
				(including antibodies and	and/or "Cardiovascular
				agonists or antagonists of the	Disorders"). Highly preferred
				invention) to mediate	indications also include
				immunomodulation and	autoimmune diseases (e.g.,

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rheumatoid arthritis, systemic lupus erythematosis, multiple serlencis and/or as described	scierosis and/or as described below) and	immunodeficiencies (e.g., as	highly preferred indications	include asthma. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia (e.g., acute	lymphoblastic leukemia, and	acute myelogenous leukemia),	lymphoma (e.g., non-	Hodgkin"s lymphoma and	Hodgkin"s disease), and/or as	described below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metanlasia and/or dvsnlasia
modulate the growth and differentiation of leukocytes. Exemplary assays that feet for	immunomodulatory proteins	evaluate the production of	and the activation of T cells.	Such assays that may be used	or routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Ye et al., J Leukoc	Biol (58(2):225-233, the	contents of each of which are	herein incorporated by	reference in its entirety.	Natural killer cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) or may be	isolated using techniques	disclosed herein or otherwise	known in the art. Natural
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			killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cellmediated cytotoxicity.	Highly preferred indications include: suppression of immune reactions to transplanted organs and tissues (e.g., bone marrow transplant); accelerating myeloid recovery; and mobilizing hematopoietic progenitor cells. Preferred indications include boosting a T cell-mediated immune response, and alternatively, suppressing a T cell-mediated immune response. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes melitus, endocarditis, Lyme Disease, and
HSKDA27	805	Regulation of	Caspase Apoptosis. Assays	allergy. A highly preferred
		apoptosis in pancreatic beta cells.	for caspase apoptosis are well known in the art and may be used or routinely modified to	indication is diabetes mellitus. An additional highly preferred indication is a complication

associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure,	diseases and disorders as described in the "Renal Disorders" section below),	disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel	impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion drowsiness	nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis,	microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment
assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and	Exemplary assays for caspase apoptosis that may be used or routinely modified to test	capase apopuosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays	disclosed in: Loweth, AC, et al., FEBS Lett, 400(3):285-8 (1997); Saini, KS, et al., Biochem Mol Biol Int,	39(6):1229-36 (1996); Krautheim, A., et al., Br J Pharmacol, 129(4):687-94 (2000); Chandra J, et al., Diabetes, 50 Suppl 1:S44-7	(2001); Suk K, et al., J Immunol, 166(7):4481-9 (2001); Tejedo J, et al., FEBS Lett, 459(2):238-43 (1999); Zhang, S., et al., FEBS Lett,
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455(3):315-20 (1999); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include RIN-m. RIN-m is a rat adherent pancreatic beta cell insulinoma cell line derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1000

HSKDA27	805	Caspase		
-		(+paclitaxel) in SW480		
HSKGN81	908	Glucose Production in H4IIE		
HSKGN81	908	SEAP in HIB/CRE		
HSKGN81	908	Stimulation of	Assays for measuring secretion	A highly preferred
		insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
		from pancreatic	the art and may be used or	An additional highly preferred
		beta cells.	routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
	<u> </u>		antibodies and agonists or	nephropathy, kidney disease
			antagonists of the invention) to	(e.g., renal failure,
			stimulate insulin secretion.	nephropathy and/or other
			For example, insulin secretion	diseases and disorders as
		-	is measured by FMAT using	described in the "Renal
			anti-rat insulin antibodies.	Disorders" section below),
			Insulin secretion from	diabetic neuropathy, nerve
			pancreatic beta cells is	disease and nerve damage
			upregulated by glucose and	(e.g., due to diabetic
			also by certain	neuropathy), blood vessel
			proteins/peptides, and	blockage, heart disease, stroke,
			disregulation is a key	impotence (e.g., due to diabetic
			component in diabetes.	neuropathy or blood vessel
			Exemplary assays that may be	blockage), seizures, mental
			used or routinely modified to	confusion, drowsiness,
			test for stimulation of insulin	nonketotic hyperglycemic-
			secretion (from pancreatic	hyperosmolar coma,
			cells) by polypeptides of the	cardiovascular disease (e.g.,
			invention (including antibodies	heart disease, atherosclerosis,

and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt described in the 2):R959-66 (1999); Li, M., et al., and other discases and disorders as described in the "Cardiovascular Disorders"		s &	ese	bancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 line established from an X-ray induced isolated from an X-ray induced transplantable insulinoma. These cells retain These cells retain These cells retain These cells retain Complications associated with insulin resistance. An additional highly preferred indications are complications associated with insulin resistance.
and agonists or antagon the invention) include a disclosed in: Ahren, B., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li,	al., Endocrinology, 138(9):3735-40 (1997); Kim K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraolia S et al. Iournal of	Biomolecular Screening, 4:193-204 (1999), the con of each of which is herein incorporated by reference	entirety. Pancreatic cells tha may be used according to the assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary	pancreatic cells that may be used according to these assay include rat INS-1 cells. INS-cells are a semi-adherent cell line established from cells isolated from an X-ray inducrat transplantable insulinoma These cells retain characteristics typical of national pancreatic beta cells including alucose inducible insulin

				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HSKGN81	908	IL-8 in SW480		
	HSLCQ82	807	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
•			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
-				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
				Proc Natl Acad Sci USA	suppressing a T cell-mediated

itional	ons	p	and	_	_	nighly	psis.	ions	ses	na,	×	,e	ly,	ous		mple,				ast,		ain,	Other	lude		stic			asia.	lude
se. Add	d indicati	nation an	lisorders,	amage in	eumatoic	ditional	ation is se	ed indicat	stic diseas	, lymphoi	ibed belo	roliferativ	dditional	d indicati	sms and	s, for exa	homa,	ma (e.g.,	na), solic	ostate, bre	ncreatic,	mach, bi	y cancer.	ations inc	iferative	re-neopla	h as, for	plasia,	l/or dyspl	ations inc
immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include
immi	high	inclu	infla	treati	patie	arthr	prefe	High	inclu	(e.g.,	and/c	nnde	Diso	high	inclu	cance	lenke	mela	malig	tumo	lung,	esop	liver	prefe	benig	disor	puoo	exan	meta	Prefe
85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.														
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ŀ	For example, insulin secretion diseases and disorders as	is measured by FMAT using described in the "Renal	anti-rat insulin antibodies. Disorders" section below),	Insulin secretion from diabetic neuropathy, nerve	pancreatic beta cells is disease and nerve damage	upregulated by glucose and (e.g., due to diabetic	es, and	disregulation is a key impotence (e.g., due to diabetic	component in diabetes. neuropathy or blood vessel	Exemplary assays that may be blockage), seizures, mental	used or routinely modified to confusion, drowsiness,	test for stimulation of insulin nonketotic hyperglycemic-	secretion (from pancreatic hyperosmolar coma,	cells) by polypeptides of the cardiovascular disease (e.g.,	invention (including antibodies heart disease, atherosclerosis,	and agonists or antagonists of microvascular disease,	the invention) include assays hypertension, stroke, and other	disclosed in: Ahren, B., et al., diseases and disorders as	 2):R959-66 (1999); Li, M., et "Cardiovascular Disorders"	al., Endocrinology, section below), dyslipidemia,	97); Kim,	K.H., et al., FEBS Lett, described in the "Endocrine	ld,	Miraglia S et. al., Journal of neuropathy, vision impairment	Biomolecular Screening, (e.g., diabetic retinopathy and	4:193-204 (1999), the contents blindness), ulcers and impaired	of each of which is herein wound healing, and infection	11. 11 Francisco Contraction Contractions of the contraction of t

				may be used according to these assays are publicly available	"Infectious Diseases" section below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
				pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HSNMC45	608	Stimulation of	Assays for measuring calcium	A highly preferred
			Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
			pancreatic beta	and may be used or routinely	An additional highly preferred
			cells.	modified to assess the ability	indication is a complication
				of polypeptides of the	associated with diabetes (e.g.,
				invention (including antibodies	diabetic retinopathy, diabetic
				and agonists or antagonists of	nephropathy, kidney disease
				the invention) to mobilize	(e.g., renal failure,
_				calcium. For example, the	nephropathy and/or other
				FLPR assay may be used to	diseases and disorders as
	•			measure influx of calcium.	described in the "Renal
				Cells normally have very low	Disorders" section below),

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diabetic neuropathy, nerve disease and nerve damage	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal
concentrations of cytosolic calcium compared to much	Extracellular factors can cause	an influx of calcium, leading to	activation of calcium	responsive signaling pathways	and alterations in cell	functions. Exemplary assays	that may be used or routinely	modified to measure calcium	flux by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Satin LS, et al.,	Endocrinology, 136(10):4589-	601 (1995); Mogami H, et al.,	Endocrinology, 136(7):2960-6	(1995); Richardson SB, et al.,	Biochem J, 288 (Pt 3):847-51	(1992); and, Meats, JE, et al.,	Cell Calcium 1989 Nov-	Dec;10(8):535-41 (1989), the	contents of each of which is	herein incorporated by	reference in its entirety.	Pancreatic cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or
									_				-				-		-	-								

			may be routinely generated.	tunnel syndrome and
			Exemplary pancreatic cells that	Dupuytren's contracture).
			may be used according to these	An additional highly preferred
			assays include HITT15 Cells.	indication is obesity and/or
			HITT15 are an adherent	complications associated with
			epithelial cell line established	obesity. Additional highly
			from Syrian hamster islet cells	preferred indications include
			transformed with SV40. These	weight loss or alternatively,
			cells express glucagon,	weight gain. Aditional
			somatostatin, and	highly preferred indications are
			glucocorticoid receptors. The	complications associated with
			cells secrete insulin, which is	insulin resistance.
			stimulated by glucose and	
			glucagon and suppressed by	
			somatostatin or	
			glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
			4339-4343, 1981.	
HSQFP66	810	Stimulation of	Assays for measuring secretion	A highly preferred
		insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
_		from pancreatic	the art and may be used or	An additional highly preferred
		beta cells.	routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease
			antagonists of the invention) to	(e.g., renal failure,
			stimulate insulin secretion.	nephropathy and/or other
			For example, insulin secretion	diseases and disorders as

au si	is measured by FMAT using	described in the "Renal
anti-r	anti-rat insulin antibodies.	Disorders" section below),
Insuli	Insulin secretion from	diabetic neuropathy, nerve
pancr	pancreatic beta cells is	disease and nerve damage
npreg	upregulated by glucose and	(e.g., due to diabetic
also b	also by certain	neuropathy), blood vessel
protei	proteins/peptides, and	blockage, heart disease, stroke,
garsib	disregulation is a key	impotence (e.g., due to diabetic
comp	component in diabetes.	neuropathy or blood vessel
Exem	Exemplary assays that may be	blockage), seizures, mental
pesn	used or routinely modified to	confusion, drowsiness,
test fo	test for stimulation of insulin	nonketotic hyperglycemic-
Secret	secretion (from pancreatic	hyperosmolar coma,
cells)	cells) by polypeptides of the	cardiovascular disease (e.g.,
inven	invention (including antibodies	heart disease, atherosclerosis,
anda	and agonists or antagonists of	microvascular disease,
the in	the invention) include assays	hypertension, stroke, and other
disclo	disclosed in: Ahren, B., et al.,	diseases and disorders as
- Am J	Am J Physiol, 277(4 Pt	described in the
2):R9	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
al., Ei	al., Endocrinology,	section below), dyslipidemia,
138(9	138(9):3735-40 (1997); Kim,	endocrine disorders (as
K.H.,	K.H., et al., FEBS Lett,	described in the "Endocrine
377(2	377(2):237-9 (1995); and,	Disorders" section below),
Mirag	Miraglia S et. al., Journal of	neuropathy, vision impairment
Biom	Biomolecular Screening,	(e.g., diabetic retinopathy and
4:193	4:193-204 (1999), the contents	blindness), ulcers and impaired
of eac	of each of which is herein	wound healing, and infection
incorp	S	(e.g., infectious diseases and
entire	entirety. Pancreatic cells that	disorders as described in the
may b	may be used according to these	"Infectious Diseases" section

				assays are publicly available	below, especially of the
				(e.g. through the ATCC)	urinary tract and skin), carnal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
-				pancreatic cells that may be	An additional highly preferred
_				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
	_			cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
	-			These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
_				pancreatic beta cells including	insulin resistance.
-				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HSRFZ57	811	Regulation of	Assays for the regulation of	A highly preferred
			transcription	transcription through the FAS	indication is diabetes mellitus.
			through the FAS	promoter element are well-	An additional highly preferred
			promoter element	known in the art and may be	indication is a complication
			in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
				invention) to activate the FAS	diseases and disorders as
				promoter element in a reporter	described in the "Renal
				construct and to regulate	Disorders" section below),
				transcription of FAS, a key	diabetic neuropathy, nerve

	enz	enzyme for lipogenesis. FAS	disease and nerve damage
	pro pro trar	transcription factors including	neuropathy), blood vessel
	SR	SREBP. Insulin increases FAS	blockage, heart disease, stroke,
-	gen	gene transcription in livers of	impotence (e.g., due to diabetic
	dia	diabetic mice. This	neuropathy or blood vessel
	stin	stimulation of transcription is	blockage), seizures, mental
	alsc	also somewhat glucose	confusion, drowsiness,
	deb	dependent. Exemplary assays	nonketotic hyperglycemic-
	tha	that may be used or routinely	hyperosmolar coma,
	om	modified to test for FAS	cardiovascular disease (e.g.,
	pro	promoter element activity (in	heart disease, atherosclerosis,
	hep	hepatocytes) by polypeptides	microvascular disease,
	oft	of the invention (including	hypertension, stroke, and other
	ant	antibodies and agonists or	diseases and disorders as
	ant	antagonists of the invention)	described in the
	inc	include assays disclosed in	"Cardiovascular Disorders"
	Xio	Xiong, S., et al., Proc Natl	section below), dyslipidemia,
	Ace	Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
	53	(2000); Roder, K., et al.,	described in the "Endocrine
	Eur	Eur J Biochem, 260(3):743-51	Disorders" section below),
	(19	(1999); Oskouian B, et al.,	neuropathy, vision impairment
	Bio	Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
	(19	(1996); Berger, et al., Gene	blindness), ulcers and impaired
	99	66:1-10 (1988); and, Cullen,	wound healing, and infection
	B.,	B., et al., Methods in Enzymol.	(e.g., infectious diseases and
	216	216:362–368 (1992), the	disorders as described in the
	con	contents of each of which is	"Infectious Diseases" section
	her	herein incorporated by	below, especially of the
	refe	reference in its entirety.	urinary tract and skin), carpal
	Hel	Hepatocytes that may be used	tunnel syndrome and

preferred and/or ated with ighly include trively, Aditional cations are ated with	nts d d such od- ders" ders"
racture). thly preferity and/city and/coriated ons inch ermativel Adit indicatio	indicatic tition (aci thosis, sthma ar breferred de di orders, isorders, ers (e.g. resis), an sorders (w. W. under y., "Blo sorders ive Disor scular ghly prefi de neopla as, for
Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Highly preferred indications include inflammation (acute and chronic), restnosis, athma and allergy. Highly preferred indications include inflammation and inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" and/or "Cardiovascular Disorders"). Highly preferred indications include neoplasms and cancers such as, for
Dupuytren's An additiona indication is complication obesity. Add preferred inc weight loss of weight gain. Highly prefer complication insulin resist	Highly I include and chroad atherosc allergy. allergy. indication inflamm inflamm inflamm cancer/t cardiova as descrational "Immun Related "Hyperg and/or" and can are a series and can and can and can and can and can are are and can are are and can are are are and can are are are and can are are are are and can are are are are are are and can are
	well- be cd to the tition tition the CAM charace urface urface urface urface urface sis, sis, scular
according to these assays, such as H4IIE cells, are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays include rat liver hepatoma cell line(s) inducible with glucocorticoids, insulin, or cAMP derivatives.	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-I expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell
according to these assa as H4IIE cells, are publavailable (e.g., through ATCC) and/or may be routinely generated. Exemplary hepatocytes may be used according assays include rat liver hepatoma cell line(s) ir with glucocorticoids, ir or cAMP derivatives.	Assays for measuring expression of VCAM known in the art and n used or routinely mod assess the ability of polypeptides of the invitation of the invention of the expression. For exam FMAT may be used to the upregulation of cell VCAM-1 expression endothelial cells. End cells are cells that line vessels, and are involving functions that include, not limited to, angioge vascular permeability, tone, and immune cell
accordinas H4III availabl ATCC) routinel Exempl may be assays i hepaton with glu or cAM	Assays express known used or assess t polyper (including agonist; inventice express FMAT the upre VCAM endothe cells are vessels, function not lim vascula tone are the presservatory.
	sells sin cells
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	Property (HI)
	811
	HSRFZ57
	HSR

			extravasation. Exemplary	example, leukemia, lymphoma,
			endothelial cells that may be	melanoma, renal cell
			used according to these assays	carcinoma, and prostate,
			include human umbilical vein	breast, lung, colon, pancreatic,
			endothelial cells (HUVEC),	esophageal, stomach, brain,
			which are available from	liver and urinary cancer. Other
			commercial sources. The	preferred indications include
			expression of VCAM	benign dysproliferative
			(CD106), a membrane-	disorders and pre-neoplastic
			associated protein, can be	conditions, such as, for
			upregulated by cytokines or	example, hyperplasia,
			other factors, and contributes	metaplasia, and/or dysplasia.
			to the extravasation of	
			lymphocytes, leucocytes and	
			other immune cells from blood	
			vessels; thus VCAM	
			expression plays a role in	
			promoting immune and	
			inflammatory responses.	
HSRFZ57	811	SEAP in Jurkat/IL4		
		promoter (antiCD3		
HSSFT08	812	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha

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production. Preferred indications include blood disorders (e.g., as described	below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"), Highly preferred indications	include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,		under "Hyperproliferative
antagonists of the invention) to regulate the serum response factors and modulate the	expression of genes involved in growth. Exemplary assays for transcription through the	SRE that may be used or routinely modified to test SRE	activity of the polypeptides of the invention (including	antibodies and agonists or	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell
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				_	-																_		
						_				_											_		

	line, which is an IL-2	Disorders"). Additionally,
	dependent suspension culture	highly preferred indications
	of T cells with cytotoxic	include neoplasms and
	activity.	cancers, such as, for example,
		leukemia, lymphoma,
		melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
_		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues,

hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as
	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
	813
	HSSGD52

		assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
	-	216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
_		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
		(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
		Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
		Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
		14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
		contents of each of which are	lymphoma, arthritis, AIDS,
		herein incorporated by	granulomatous disease,
		reference in its entirety. Mast	inflammatory bowel disease,
		cells that may be used	sepsis, neutropenia,
		according to these assays are	neutrophilia, psoriasis,
		publicly available (e.g.,	suppression of immune
		through the ATCC).	reactions to transplanted
		Exemplary human mast cells	organs and tissues, hemophilia,

			that may be used according to these assays include the HMC-1 cell line, which is an	hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
			immature human mast cell line established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
Heegher	813	Activation of	This renorter accouragement	Highly preferred indications
76706611	610	transcription	activation of the NFAT	include allergy, asthma, and
		through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and
			activation of transcription	inflammatory disorders.
			through the Nuclear Factor of	Preferred indications also
			Activated T cells (NFAT)	include blood disorders (e.g.,
			response element are well-	as described below under
			known in the art and may be	"Immune Activity", "Blood-
			used or routinely modified to	Related Disorders", and/or
			assess the ability of	"Cardiovascular Disorders").
			polypeptides of the invention	Preferred indications include
			(including antibodies and	autoimmune diseases (e.g.,
			agonists or antagonists of the	rheumatoid arthritis, systemic
			invention) to regulate NFAT	lupus erythematosis, multiple
			transcription factors and	sclerosis and/or as described
			modulate expression of genes	below) and
			involved in	immunodeficiencies (e.g., as

		immunomodulatory functions.	described below). Preferred
		Exemplary assays for	indications include neoplastic
		transcription through the	diseases (e.g., leukemia,
		NFAT response element that	lymphoma, melanoma,
		may be used or routinely	prostate, breast, lung, colon,
		modified to test NFAT-	pancreatic, esophageal,
		response element activity of	stomach, brain, liver, and
		polypeptides of the invention	urinary tract cancers and/or as
		(including antibodies and	described below under
	-	agonists or antagonists of the	"Hyperproliferative
•		invention) include assays	Disorders"). Other preferred
	•	disclosed in Berger et al., Gene	indications include benign
		66:1-10 (1998); Cullen and	dysproliferative disorders and
		Malm, Methods in Enzymol	pre-neoplastic conditions, such
		216:362-368 (1992); Henthorn	as, for example, hyperplasia,
		et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
		85:6342-6346 (1988); De Boer	Preferred indications include
		et al., Int J Biochem Cell Biol	anemia, pancytopenia,
		31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
		et al., J Immunol	leukemias, Hodgkin's disease,
		165(12):7215-7223 (2000);	acute lymphocytic anemia
		Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	-	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
		16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
		al., J Exp Med 188:527-537	granulomatous disease,
		(1998), the contents of each of	inflammatory bowel disease,
		which are herein incorporated	sepsis, neutropenia,
		by reference in its entirety.	neutrophilia, psoriasis,
		Mast cells that may be used	suppression of immune
		according to these assays are	reactions to transplanted
		publicly available (e.g.,	organs and tissues, hemophilia,

hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	l o
through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the Cell Titer-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP
	Proliferation of preadipose cells (such as 3T3-L1 cells)
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"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,
genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.
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	malignant glioma), solid
	tumors, and prostate, breast,
	lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	benign dysproliferative
	disorders and pre-neoplastic
 	conditions, such as, for
 	example, hyperplasia,
 	metaplasia, and/or dysplasia.
 	Preferred indications include
 	anemia, pancytopenia,
	leukopenia, thrombocytopenia,
 	Hodgkin's disease, acute
	lymphocytic anemia (ALL),
	plasmacytomas, multiple
	myeloma, Burkitt's lymphoma,
	arthritis, AIDS, granulomatous
 	disease, inflammatory bowel
	disease, neutropenia,
	neutrophilia, psoriasis,
	suppression of immune
	reactions to transplanted
 	organs and tissues, hemophilia,
 	hypercoagulation, diabetes
	mellitus, endocarditis,
	meningitis, Lyme Disease,
 	cardiac reperfusion injury, and
 	asthma and allergy. An
	additional preferred indication